		Mol Endocrinol, 13(8):1305-	section below). dyslinidemia.
		17 (1999); Filipsson, K., et al.,	endocrine disorders (as
	7	Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
		(1998); Olson, L.K., et al., J	Disorders" section below),
	<u> </u>	Biol Chem, 271(28):16544-52	neuropathy, vision impairment
		(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
	<u>f</u>	Journal of Biomolecular	blindness), ulcers and impaired
		Screening, 4:193-204 (1999),	wound healing, and infection
		the contents of each of which	(e.g., infectious diseases and
		is herein incorporated by	disorders as described in the
	ı	reference in its entirety.	"Infectious Diseases" section
	4	Pancreatic cells that may be	below, especially of the
	p	used according to these assays	urinary tract and skin), carpal
		are publicly available (e.g.,	tunnel syndrome and
		through the ATCC) and/or	Dupuytren's contracture).
		may be routinely generated.	An additional highly preferred
-	<u> </u>	Exemplary pancreatic cells that	indication is obesity and/or
	u	may be used according to these	complications associated with
	<u>a</u>	assays include HITT15 Cells.	obesity. Additional highly
		HITT15 are an adherent	preferred indications include
	<u> </u>	epithelial cell line established	weight loss or alternatively,
	4	from Syrian hamster islet cells	weight gain. Additional highly
	-	transformed with SV40. These	preferred indications are
	<u> </u>	cells express glucagon,	complications associated with
	S	somatostatin, and	insulin resistance.
	20	glucocorticoid receptors. The	
	3	cells secrete insulin, which is	
	S	stimulated by glucose and	
	50	glucagon and suppressed by	
	S	somatostatin or	
	50	glucocorticoids. ATTC# CRL-	

				1777 Refs. Lord and	
				Asherolt. Biochem. J. 219. 547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
<u>-</u>	HNFJF07	731	Regulation of	Assays for the regulation of	A highly preferred indication
			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other
				DMEF1 response element in a	diseases and disorders as
				reporter construct (such as that	described in the "Renal
				containing the GLUT4	Disorders" section below),
				promoter) and to regulate	diabetic neuropathy, nerve
				insulin production. The	disease and nerve damage
	-			DMEF1 response element is	(e.g., due to diabetic
				present in the GLUT4	neuropathy), blood vessel
				promoter and binds to MEF2	blockage, heart disease, stroke,
	-			transcription factor and another	impotence (e.g., due to diabetic
				transcription factor that is	neuropathy or blood vessel
				required for insulin regulation	blockage), seizures, mental
				of Glut4 expression in skeletal	confusion, drowsiness,
				muscle. GLUT4 is the primary	nonketotic hyperglycemic-
	•			insulin-responsive glucose	hyperosmolar coma,
				transporter in fat and muscle	cardiovascular disease (e.g.,
				tissue. Exemplary assays that	heart disease, atherosclerosis,

may	may be used or routinely	microvascular disease,
moo	modified to test for DMEF1	hypertension, stroke, and other
 rest	response element activity (in	diseases and disorders as
adij	adipocytes and pre-adipocytes)	described in the
 by 1	by polypeptides of the	"Cardiovascular Disorders"
inve	invention (including antibodies	section below), dyslipidemia,
 and	and agonists or antagonists of	endocrine disorders (as
 the	the invention) include assays	described in the "Endocrine
 disc	disclosed inThai, M.V., et al., J	Disorders" section below),
 Bio	Biol Chem, 273(23):14285-92	neuropathy, vision impairment
 (1)	(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
 Che	Chem, 275(21):16323-8	blindness), ulcers and impaired
 (20	(2000); Liu, M.L., et al., J Biol	wound healing, and infection
 Che	Chem, 269(45):28514-21	(e.g., infectious diseases and
(1)	(1994); "Identification of a 30-	disorders as described in the
 base	base pair regulatory element	"Infectious Diseases" section
and	and novel DNA binding	below, especially of the
pro	protein that regulates the	urinary tract and skin). An
unu	human GLUT4 promoter in	additional highly preferred
 tran	transgenic mice", J Biol Chem.	indication is obesity and/or
 200	2000 Aug 4;275(31):23666-73;	complications associated with
 Ber	Berger, et al., Gene 66:1-10	obesity. Additional highly
 (19	(1988); and, Cullen, B., et al.,	preferred indications include
 Mei	Methods in Enzymol.	weight loss or alternatively,
 216	216:362–368 (1992), the	weight gain. Additional highly
 con	contents of each of which is	preferred indications are
 here	herein incorporated by	complications associated with
 refe	reference in its entirety.	insulin resistance.
 Adi	Adipocytes and pre-adipocytes	
that	that may be used according to	
thes	these assays are publicly	

			available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	
HNFJF07	731	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic

		culture based on quantitation	neuropathy), blood vessel
		of the ATP present which	blockage, heart disease, stroke,
		signals the presence of	impotence (e.g., due to diabetic
		metabolically active cells.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test regulation of viability and	nonketotic hyperglycemic-
		proliferation of pancreatic beta	hyperosmolar coma,
		cells by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
	~	disclosed in: Friedrichsen BN,	diseases and disorders as
		et al., Mol Endocrinol,	described in the
		15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
		MA, et al., Endocrinology,	section below), dyslipidemia,
	~	139(4):1494-9 (1998); Hugl	endocrine disorders (as
	-	SR, et al., J Biol Chem 1998	described in the "Endocrine
	-	Jul 10;273(28):17771-9	Disorders" section below),
	_	(1998), the contents of each of	neuropathy, vision impairment
	~~	which is herein incorporated	(e.g., diabetic retinopathy and
		by reference in its entirety.	blindness), ulcers and impaired
	-	Pancreatic cells that may be	wound healing, and infection
		used according to these assays	(e.g., infectious diseases and
-	-	are publicly available (e.g.,	disorders as described in the
		through the ATCC) and/or	"Infectious Diseases" section
		may be routinely generated.	below, especially of the
		Exemplary pancreatic cells that	urinary tract and skin), carpal
		may be used according to these	tunnel syndrome and
		assays include rat INS-1 cells.	Dupuytren's contracture). An
		INS-1 cells are a semi-	additional highly preferred

			adherent cell line established	indication is obesity and/or
			from cells isolated from an X-	complications associated with
			ray induced rat transplantable	obesity. Additional highly
			insulinoma. These cells retain	preferred indications include
			characteristics typical of native	weight loss or alternatively,
			pancreatic beta cells including	weight gain. Additional highly
			glucose inducible insulin	preferred indications are
			secretion. References: Asfari	complications associated with
			et al. Endocrinology 1992	insulin resistance.
			130:167.	
HNFJF07	731	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth. Exemplary assays	Activity", "Blood-Related
			for transcription through the	Disorders", and/or
			SRE that may be used or	"Cardiovascular Disorders"),
			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
			antagonists of the invention)	Crohn"s disease, multiple

include assays disclosed in sclerosis and/or as described Berger et al., Gene 66:1-10 (1998); Cullen and Malm., (eg. as described below), Methods in Enzymol 216:362 - boosting a T cell-mediated immune response, and Proc Natl Acad Sci USA (1992); Henthom et al., Sci 542-6346 (1988); and immune response. Additional Black et al., Virus Genes incuperated by reference in its entirety. Therefore in its entirety. The patients with rheumatory disorders, and cells that may be used according to these assays are through the ATCC. Exemplary mouse T cells that may be used according to these assays are billine, which is an IL-2 Disorders.) Additionally, dependent suspension culture index indications of T cells with cytotoxic encers, such as, for example, line, which is an IL-2 Disorders?). Additionally, elegendent suspension culture indications include neoplasms and cancers, such as, for example, lenkemia, lymphoma, malphanel activity. Exemplary mouse T cells with cytotoxic and prostate, breast, line, which is an IL-2 Disorders?). Additionally, elegendent suspension culture include neoplasms and cancers, such as, for example, lenkemia, lymphoma, malphanel malignant glioma), solid tumors, and prostate, breast, lung, colon, parcreatic, esophageal, somach, parin, preferred indications include esophageal, somach, parin, preferred indications include according to these malignant gliomal, solid tumors, and prostate, breast, lung, colon, parcreatic, esophageal, somach, parin, liver and unirary cancer. Other preferred indications include according indications include the colon, parcreatic, esophageal, somach, parin, liver and unirary cancer. Other preferred indications include the colon, parcreatic, esophageal, somach, parin, parcreatic, postate preferred indications include the colon part and prostate, breast, part and prostate, breast, preferred indications in includence preferred indications in includence preferred indications in includence preferred in
incl Berry (199) Met 12(7) 85:6 86:6

				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HNFJF07	731	Stimulation of	Assays for measuring secretion	A highly preferred
		insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
		from pancreatic	the art and may be used or	An additional highly preferred

beta cells.	routinely modified to assess	indication is a complication
	the ability of polypeptides of	associated with diabetes (e.g.,
	the invention (including	diabetic retinopathy, diabetic
	antibodies and agonists or	nephropathy, kidney disease
	antagonists of the invention) to	(e.g., renal failure,
	stimulate insulin secretion.	nephropathy and/or other
	For example, insulin secretion	diseases and disorders as
	is measured by FMAT using	described in the "Renal
	anti-rat insulin antibodies.	Disorders" section below),
	Insulin secretion from	diabetic neuropathy, nerve
	pancreatic beta cells is	disease and nerve damage
	upregulated by glucose and	(e.g., due to diabetic
	also by certain	neuropathy), blood vessel
	proteins/peptides, and	blockage, heart disease, stroke,
	disregulation is a key	impotence (e.g., due to diabetic
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al., Endocrinology,	section below), dyslipidemia,
	138(9):3735-40 (1997); Kim,	endocrine disorders (as
	K.H., et al., FEBS Lett,	described in the "Endocrine
	377(2):237-9 (1995); and,	Disorders" section below),

			Miraelia S et. al., Journal of	neuropathy, vision impairment
			Biomolecular Screening,	(e.g., diabetic retinopathy and
			4:193-204 (1999), the contents	blindness), ulcers and impaired
			of each of which is herein	wound healing, and infection
			incorporated by reference in its	(e.g., infectious diseases and
			entirety. Pancreatic cells that	disorders as described in the
			may be used according to these	"Infectious Diseases" section
			assays are publicly available	below, especially of the
			(e.g., through the ATCC)	urinary tract and skin), carpal
			and/or may be routinely	tunnel syndrome and
			generated. Exemplary	Dupuytren's contracture).
			pancreatic cells that may be	An additional highly preferred
			used according to these assays	indication is obesity and/or
			include rat INS-1 cells. INS-1	complications associated with
			cells are a semi-adherent cell	obesity. Additional highly
			line established from cells	preferred indications include
			isolated from an X-ray induced	weight loss or alternatively,
			rat transplantable insulinoma.	weight gain. Aditional
			These cells retain	highly preferred indications are
			characteristics typical of native	complications associated with
			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
			secretion. References: Asfari	
			et al. Endocrinology 1992	
			130:167.	
HNGAK47	732	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
		Apoptosis	caspase apoptosis are well	embodiment of the invention
			known in the art and may be	includes a method for
			used or routinely modified to	stimulating endothelial cell
			assess the ability of	growth. An alternative highly
			polypeptides of the invention	preferred embodiment of the

(i)	(including antibodies and	invention includes a method
38	agonists or antagonists of the	for inhibiting endothelial cell
ui.	invention) to promote caspase	growth. A highly preferred
Id	protease-mediated apoptosis.	embodiment of the invention
<u> </u>	Induction of apoptosis in	includes a method for
15	endothelial cells supporting the	stimulating endothelial cell
20	vasculature of tumors is	proliferation. An alternative
288	associated with tumor	highly preferred embodiment
re	regression due to loss of tumor	of the invention includes a
[9]	blood supply. Exemplary	method for inhibiting
as	assays for caspase apoptosis	endothelial cell proliferation.
th	that may be used or routinely	A highly preferred
m	modified to test capase	embodiment of the invention
	apoptosis activity of	includes a method for
)d	polypeptides of the invention	stimulating apoptosis of
<u>.i.)</u>	(including antibodies and	endothelial cells. An
	agonists or antagonists of the	alternative highly preferred
- i	invention) include the assays	embodiment of the invention
<u> </u>	disclosed in Lee et al., FEBS	includes a method for
<u> </u>	Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
<u>Z</u>	Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
20	209-218 (2000); and Karsan	A highly preferred
an	and Harlan, J Atheroscler	embodiment of the invention
	Thromb 3(2): 75-80 (1996);	includes a method for
th	the contents of each of which	stimulating angiogenisis. An
ar	are herein incorporated by	alternative highly preferred
re	reference in its entirety.	embodiment of the invention
	Endothelial cells that may be	includes a method for
sn	used according to these assays	inhibiting angiogenesis. A
ar	are publicly available (e.g.,	highly preferred embodiment
th	through commercial sources).	of the invention includes a

such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,
			-						-																		,			
																														-

pancreatic, esophageal, stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	Iymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),
		•							•••										-							_			
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implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis,	cerebrovascular disease, renal diseases such as acute renal	failure, and osteoporosis. Additional highly preferred	graft rejection, diabetic or	oner reunopaunes, unouncouc and coagulative disorders,	vascularitis, lymph angiogenesis, sexual disorders.	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions. Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic
																		-			
													•								
															-						

lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of
	Activation of transcription through serum response element in immune cells (such as T-cells).
	732
	HNGAK47

the invention (including (e.g., rheumatoid arthritis,	antibodies and agonists or systemic lupus erythematosis,	(u)	include assays disclosed in sclerosis and/or as described	Berger et al., Gene 66:1-10 below), immunodeficiencies	-5	368 (1992); Henthorn et al., immune response, and	Proc Natl Acad Sci USA suppressing a T cell-mediated	85:6342-6346 (1988); and immune response. Additional	Black et al., Virus Genes highly preferred indications	 content of each of which are inflammatory disorders, and	herein incorporated by treating joint damage in	reference in its entirety. T patients with rheumatoid	cells that may be used arthritis. An additional highly	s are	s.g.,	through the ATCC). include neoplastic diseases	 may be used according to these and/or as described below	assays include the CTLL cell under "Hyperproliferative	line, which is an IL-2 Disorders"). Additionally,	dependent suspension culture highly preferred indications	of T cells with cytotoxic include neoplasms and	activity. cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,

esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia,	neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation,	diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
		,			

	HNGBC07	733	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
-			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
		-		expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
		-		transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
		-		modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn's disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
		***		the invention) include assays	(e.g., as described below),
_			_	disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
				Malm, Methods in Enzymol	suppressing a T cell-mediated
		-		216:362-368 (1992); Henthorn	immune response. Additional
				et al., Proc Natl Acad Sci USA	highly preferred indications
				85:6342-6346 (1988); Benson	include inflammation and
				et al., J Immunol 153(9):3862-	inflammatory disorders, and

3873 (1994); and Black et al., Virus Genes 12(2):105-117	treating joint damage in patients with rheumatoid
(1997), the content of each of	arthritis. An additional highly
which are herein incorporated	preferred indication is sepsis.
by reference in its entirety. T	Highly preferred indications
cells that may be used	include neoplastic diseases
according to these assays are	(e.g., leukemia, lymphoma,
publicly available (e.g.,	and/or as described below
through the ATCC).	under "Hyperproliferative
Exemplary T cells that may be	Disorders"). Additionally,
used according to these assays	highly preferred indications
 include the NK-YT cell line,	include neoplasms and
which is a human natural killer	cancers, such as, for example,
cell line with cytolytic and	leukemia, lymphoma,
cytotoxic activity.	melanoma, glioma (e.g.,
	malignant glioma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	Preferred indications include
	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	Hodgkin's disease, acute
	lymphocytic anemia (ALL),

plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	734
	HNGDG40

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention
example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127- 133 (1974), which is herein incorporated by reference in its	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
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	HNGDG40

				antagonists of the invention) to lincludes a method for	includes a method for
				antagometro of inhibit cell	stimulating endothelial cell
_				promote of minor cen	Summing chacking con
				proliferation, activation, and	proliferation. An alternative
				apoptosis. Exemplary assays	highly preferred embodiment
				for JNK and p38 kinase	of the invention includes a
-				activity that may be used or	method for inhibiting
			***	routinely modified to test JNK	endothelial cell proliferation.
				and p38 kinase-induced	A highly preferred
				activity of polypeptides of the	embodiment of the invention
_	_			invention (including antibodies	includes a method for
	_			and agonists or antagonists of	stimulating apoptosis of
				the invention) include the	endothelial cells. An
_				assays disclosed in Forrer et	alternative highly preferred
				al., Biol Chem 379(8-9):1101-	embodiment of the invention
	,	-		1110 (1998); Gupta et al., Exp	includes a method for
				Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
				(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
				Soc Symp 64:29-48 (1999);	A highly preferred
				Chang and Karin, Nature	embodiment of the invention
-				410(6824):37-40 (2001); and	includes a method for
	-			Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	-			Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
				the contents of each of which	alternative highly preferred
				are herein incorporated by	embodiment of the invention
				reference in its entirety.	includes a method for
_				Endothelial cells that may be	inhibiting (e.g., decreasing) the
				used according to these assays	activation of and/or
				are publicly available (e.g.,	inactivating endothelial cells.
		_		through the ATCC).	A highly preferred
				Exemplary endothelial cells	embodiment of the invention
	-			that may be used according to	includes a method for

	these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
	(no vec), willen ale endothelial cells which line	includes a method for
- Ne	venous blood vessels, and are	inhibiting angiogenesis. A
ni	involved in functions that	highly preferred embodiment
ni	include, but are not limited to,	of the invention includes a
an	angiogenesis, vascular	method for reducing cardiac
be	permeability, vascular tone,	hypertrophy. An alternative
an	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
-		preferred indications include
		neoplastic diseases (e.g., as
		described below under
-		"Hyperproliferative
 		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
 		and atherosclerotic vascular
		disease, diabetic nephropathy,
 -		intracardiac shunt, cardiac
		hypertrophy, myocardial
 		infarction, chronic
		hemodynamic overload, and/or

as described below under	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,
																				-				-			_		
															-														
												_									-					_			

	8	angiosarcoma.
	q	haemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
	<u> </u>	preferred indications also
		include cancers such as,
	<u>a.</u>	prostate, breast, lung, colon,
	<u>d</u>	pancreatic, esophageal,
	S	stomach, brain, liver, and
	n	urinary cancer. Preferred
	- 11	indications include benign
	'	dysproliferative disorders and
	<u>a</u>	pre-neoplastic conditions, such
	8	as, for example, hyperplasia,
	<u>u</u>	metaplasia, and/or dysplasia.
	<u> </u>	Highly preferred indications
	a	also include arterial disease,
	S	such as, atherosclerosis,
	q	hypertension, coronary artery
	þ	disease, inflammatory
	>	vasculitides, Reynaud"s
	'	disease and Reynaud"s
	<u>d</u>	phenomenom, aneurysms,
		restenosis; venous and
-	<u> </u>	lymphatic disorders such as
		thrombophlebitis,
	<u></u>	lymphangitis, and
	<u></u>	lymphedema; and other
	>	vascular disorders such as
	<u>d</u>	peripheral vascular disease,
	В	and cancer. Highly

		preferred indications also
		include trauma such as
		wounds, burns, and injured
		tissue (e.g., vascular injury
		such as, injury resulting from
		balloon angioplasty, and
		atheroschlerotic lesions),
		implant fixation, scarring,
		ischemia reperfusion injury,
		rheumatoid arthritis,
		cerebrovascular disease, renal
		diseases such as acute renal
	 	failure, and osteoporosis.
		Additional highly preferred
		indications include stroke,
		graft rejection, diabetic or
		other retinopathies, thrombotic
		and coagulative disorders,
		vascularitis, lymph
		angiogenesis, sexual disorders,
		age-related macular
		degeneration, and treatment
-		/prevention of endometriosis
	 	and related conditions.
		Additional highly preferred
		indications include fibromas,
		heart disease, cardiac arrest,
	 -	heart valve disease, and
		vascular disease.
		Preferred indications include
		blood disorders (e.g., as

		factors and modulate the	disorders (e.g., as described
		expression of genes involved	below under "Immune
		in growth. Exemplary assays	Activity", "Blood-Related
		for transcription through the	Disorders", and/or
		SRE that may be used or	"Cardiovascular Disorders"),
		routinely modified to test SRE	Highly preferred indications
		activity of the polypeptides of	include autoimmune diseases
		the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
	•	antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
	-	85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
_		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
	,	according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
_		through the ATCC).	include neoplastic diseases
-		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative
·		line, which is an IL-2	Disorders"). Additionally,
		dependent suspension culture	highly preferred indications

	tumors, and prostate, breast, lung, colon, pancreatic,	esopnageai, stomach, orain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	piasmacytomas, muiupie myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diahetes mellitus, endocarditis.
of T cells with cytotoxic activity.																			

				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HNGFR31	736	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
			of insulin are well-known in	is diabetes mellitus. An
			the art and may be used or	additional highly preferred
			routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
			is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
			disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-
			secretion (from pancreatic	hyperosmolar coma,
			cells) by polypeptides of the	cardiovascular disease (e.g.,

		invention (including antibodies	heart disease, atherosclerosis,
			microvascular disease,
		the invention) include assays	hypertension, stroke, and other
-	 ,	disclosed in: Shimizu, H., et	diseases and disorders as
		al., Endocr J, 47(3):261-9	described in the
-	-	(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
		Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
_		17 (1999); Filipsson, K., et al.,	endocrine disorders (as
		Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
		(1998); Olson, L.K., et al., J	Disorders" section below),
		Biol Chem, 271(28):16544-52	neuropathy, vision impairment
		(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
		Journal of Biomolecular	blindness), ulcers and impaired
	 ·	Screening, 4:193-204 (1999),	wound healing, and infection
		the contents of each of which	(e.g., infectious diseases and
		is herein incorporated by	disorders as described in the
		reference in its entirety.	"Infectious Diseases" section
		Pancreatic cells that may be	below, especially of the
		used according to these assays	urinary tract and skin), carpal
		are publicly available (e.g.,	tunnel syndrome and
		through the ATCC) and/or	Dupuytren's contracture).
		may be routinely generated.	An additional highly preferred
		Exemplary pancreatic cells that	indication is obesity and/or
		may be used according to these	complications associated with
		assays include HITT15 Cells.	obesity. Additional highly
		HITT15 are an adherent	preferred indications include
-		epithelial cell line established	weight loss or alternatively,
		from Syrian hamster islet cells	weight gain. Additional highly
	 	transformed with SV40. These	preferred indications are
		cells express glucagon,	complications associated with
		somatostatin, and	insulin resistance.

			glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
HNGIJ31	737	Activation of transcription through cAMP response element in immune cells (such as T-cells).	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription texpression	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below),
			element that may be used or routinely modified to test cAMP-response element	boosting a T cell-mediated immune response, and suppressing a T cell-mediated

		activity of polynentides of the	immune response. Additional
		invention (including antibodies	preferred indications include
		and agonists or antagonists of	inflammation and
		the invention) include assays	inflammatory disorders.
		disclosed in Berger et al., Gene	Highly preferred indications
		66:1-10 (1998); Cullen and	include neoplastic diseases
		Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
		216:362-368 (1992); Henthorn	and/or as described below
		et al., Proc Natl Acad Sci USA	under "Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Genes 15(2):105-117	indications include neoplasms
		(1997); and Belkowski et al., J	and cancers, such as, for
		Immunol 161(2):659-665	example, leukemia, lymphoma
		(1998), the contents of each of	(e.g., T cell lymphoma,
		which are herein incorporated	Burkitt's lymphoma, non-
	-	by reference in its entirety. T	Hodgkins lymphoma,
		cells that may be used	Hodgkin"s disease),
		according to these assays are	melanoma, and prostate,
		publicly available (e.g.,	breast, lung, colon, pancreatic,
		through the ATCC).	esophageal, stomach, brain,
		Exemplary mouse T cells that	liver and urinary cancer. Other
-		may be used according to these	preferred indications include
		assays include the CTLL cell	benign dysproliferative
		line, which is a suspension	disorders and pre-neoplastic
		culture of IL-2 dependent	conditions, such as, for
		cytotoxic T cells.	example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
	_		anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			acute lymphocytic anemia

			,	(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and
HNGIJ31	737	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammation and inflammation and inflammatory disorders.

	evaluate the production of cell	Preferred indications include
	oc Hous markets	blood disorders (e a as
	Suilace markers, such as	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
	monocyte chemoattractant	described below under
	protein (MCP), and the	"Immune Activity", "Blood-
	activation of monocytes and T	Related Disorders", and/or
	cells. Such assays that may be	"Cardiovascular Disorders").
	used or routinely modified to	Highly preferred indications
	test immunomodulatory and	include autoimmune diseases
	diffferentiation activity of	(e.g., rheumatoid arthritis,
	polypeptides of the invention	systemic lupus erythematosis,
	(including antibodies and	multiple sclerosis and/or as
	agonists or antagonists of the	described below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Miraglia et al., J	described below). Preferred
	Biomolecular Screening 4:193-	indications also include
	204(1999); Rowland et al.,	anemia, pancytopenia,
	"Lymphocytes: a practical	leukopenia, thrombocytopenia,
	approach" Chapter 6:138-160	Hodgkin's disease, acute
	(2000); Satthaporn and	lymphocytic anemia (ALL),
	Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
	45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
	158:2919-2925 (1997), the	disease, inflammatory bowel
-	contents of each of which are	disease, sepsis, neutropenia,
	herein incorporated by	neutrophilia, psoriasis,
	reference in its entirety.	suppression of immune
	Human dendritic cells that may	reactions to transplanted
	be used according to these	organs and tissues,
	assays may be isolated using	hemophilia, hypercoagulation,
	techniques disclosed herein or	diabetes mellitus, endocarditis,
	otherwise known in the art.	meningitis (bacterial and

anti-rat insulin antibodies.	Disorders" section below).
Insulin secretion from	diabetic neuropathy, nerve
pancreatic beta cells is	disease and nerve damage
upregulated by glucose and	(e.g., due to diabetic
also by certain	neuropathy), blood vessel
proteins/peptides, and	blockage, heart disease, stroke,
disregulation is a key	impotence (e.g., due to diabetic
component in diabetes.	neuropathy or blood vessel
Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
test for stimulation of insulin	nonketotic hyperglycemic-
secretion (from pancreatic	hyperosmolar coma,
cells) by polypeptides of the	cardiovascular disease (e.g.,
 invention (including antibodies	heart disease, atherosclerosis,
 and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Ahren, B., et al.,	diseases and disorders as
 Am J Physiol, 277(4 Pt	described in the
(2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
al., Endocrinology,	section below), dyslipidemia,
138(9):3735-40 (1997); Kim,	endocrine disorders (as
K.H., et al., FEBS Lett,	described in the "Endocrine
377(2):237-9 (1995); and,	Disorders" section below),
 Miraglia S et. al., Journal of	neuropathy, vision impairment
Biomolecular Screening,	(e.g., diabetic retinopathy and
4:193-204 (1999), the contents	blindness), ulcers and impaired
of each of which is herein	wound healing, and infection
 incorporated by reference in its	(e.g., infectious diseases and
 entirety. Pancreatic cells that	disorders as described in the
may be used according to these	"Infectious Diseases" section
assays are publicly available	below, especially of the

			(e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
HNGIJ31	737	Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival.	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle

cell proliferation is stimulated. An alternative highly preferred embodiment of the invention	includes a method for inhibiting muscle cell	proliferation. In a specific	embodiment, skeletal muscle cell proliferation is inhibited.	A preferred embodiment of	method for stimulating muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is	stimulated. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is	inhibited. Highly preferred	indications include disorders of	the musculoskeletal system.	Preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), endocrine	disorders (e.g., as described	below under "Endocrine
Exemplary assays for PI3 kinase activity that may be used or routinely modified to	test PI3 kinase-induced activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of the invention) include assays	disclosed in Forrer et al., Biol	(1998): Nikoulina et al	Diabetes 49(2):263-271	(2000); and Schreyer et al.,	Diabetes 48(8):1662-1666	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Rat myoblast cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary rat myoblast cells	that may be used according to	these assays include L6 cells.	L6 is an adherent rat myoblast	cell line, isolated from primary	cultures of rat thigh muscle,	that fuses to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.
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Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence
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												_									_				-					

(e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,	nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infections (e.g., infectious diseases and disorders as described in the	below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with

obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Additonal highly preferred indications are disorders of the musculoskeletal system including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital	cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other

				preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.
HNGJE50	738	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6	A highly preferred embodiment of the invention includes a method for
,			participates in IL-4 induced IgE production and increases IgA production (IgA plays a	stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a
			IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune	method for inhibiting (e.g., reducing) IL-6 production. A highly preferrred indication is
			disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases.	the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as
			and differentiation factor proteins produced by a large variety of cells where the expression level is strongly	described below under "Immune Activity", "Blood- Related Disorders", and/or "Cardiovascular Disorders"),
			regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of	and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g.,
			polypeptides of the invention (including antibodies and	rheumatoid arthritis, systemic lupus erythematosis, multiple

sclerosis and/or as described below) and immunodeficiencies (e.g., as	described below). Highly preferred indications also	include boosting a B cell- mediated immune response	and alternatively suppressing a B cell-mediated immune	response. Highly preferred	indications include inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described		"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and
agonists or antagonists of the invention) to mediate immunomodulation and	differentiation and modulate T cell proliferation and function.	Exemplary assays that test for immunomodulatory proteins	evaluate the production of cytokines. such as IL-6, and	the stimulation and	upregulation of T cell proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.
		-																						
						-					-										-			
													-											

				Human dendritic cells that may be used according to these	urinary cancer. Other preferred indications include benign
				assays may be isolated using	dysproliferative disorders and
_				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
,				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
-				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
		!	!		Disease").
	HNGJE50	738	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred

neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired	wound healing, and infection (e.g., infectious diseases and disorders as described in the	"Infectious Diseases" section below, especially of the	urinary tract and skin), carpai tunnel syndrome and Dupuytren's contracture).	An additional nightly preferred indication is obesity and/or	complications associated with obesity. Additional highly	preferred indications include weight loss or alternatively,	weight gain. Additional highly preferred indications are	complications associated with insulin resistance.						
2 .	Screening, 4:193-204 (1999), we the contents of each of which is herein incorporated by		S.		o these	HITT15 are an adherent prepithelial cell line established we	from Syrian hamster islet cells we transformed with SV40. These pr	cells express glucagon, co	glucocorticoid receptors. The cells secrete insulin, which is	stimulated by glucose and glucagon and suppressed by	somatostatin or glucocorticoids. ATTC# CR1	1777 Refs: Lord and	Ashcroft. Biochem. J. 219:	Natl. Acad. Sci. USA 78:
Bic (19)	Scr the is b	refe	use are thr	ma Exc	ma	HIT	fron	cell	glu cell	stir	son la	771	AS	Nai

				4339-4343, 1981.	
	HNGJT54	739	Activation of	Assays for the activation of	Preferred indications include
			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
_			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP	Disease"). Preferred
				and regulate CREB	indications include
			,	transcription factors, and	autoimmune diseases (e.g.,
				modulate expression of genes	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, multiple
				cell functions. Exemplary	sclerosis and/or as described
				assays for transcription	below), immunodeficiencies
			-	through the cAMP response	(e.g., as described below),
				element that may be used or	boosting a T cell-mediated
				routinely modified to test	immune response, and
				cAMP-response element	suppressing a T cell-mediated
				activity of polypeptides of the	immune response. Additional
				invention (including antibodies	preferred indications include
				and agonists or antagonists of	inflammation and
				the invention) include assays	inflammatory disorders.
				disclosed in Berger et al., Gene	Highly preferred indications
				66:1-10 (1998); Cullen and	include neoplastic diseases
				Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
				216:362-368 (1992); Henthorn	and/or as described below
				et al., Proc Natl Acad Sci USA	under "Hyperproliferative
				85:6342-6346 (1988); Black et	Disorders"). Highly preferred

					diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
1	HNGJT54	739	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated
				85:6342-6346 (1988); and	immune response. Additional

	Black et a	Black et al Virus Genes	highly preferred indications
	201:(0/21		include inflammation and
	(2).(2).1	5-11/ (1991), ale	
	content of	content of each of which are	inflammatory disorders, and
	herein inc		treating joint damage in
	reference	reference in its entirety. T	patients with rheumatoid
	cells that	cells that may be used	arthritis. An additional highly
	according	s are	preferred indication is sepsis.
	publicly a	publicly available (e.g.,	Highly preferred indications
	through th	through the ATCC).	include neoplastic diseases
	Exemplar	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be us		and/or as described below
	assays inc	LL cell	under "Hyperproliferative
	line, whic	line, which is an IL-2	Disorders"). Additionally,
	dependen	culture	highly preferred indications
	of T cells		include neoplasms and
	activity.		cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
-			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,

leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly
	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the
	Production of MCP-1
	739
	HNGJT54

	invention (including antibodies	preferred indication is
	and agonists or antagonists of	infection (e.g., an infectious
***	the invention) to mediate	disease as described below
	immunomodulation, induce	under "Infectious Disease").
<u>.</u>	chemotaxis, and modulate	Additional highly preferred
	immune cell activation.	indications include
_	Exemplary assays that test for	inflammation and
	immunomodulatory proteins	inflammatory disorders.
-	evaluate the production of cell	Preferred indications include
	surface markers, such as	blood disorders (e.g., as
	monocyte chemoattractant	described below under
-	protein (MCP), and the	"Immune Activity", "Blood-
	activation of monocytes and T	Related Disorders", and/or
	cells. Such assays that may be	"Cardiovascular Disorders").
	used or routinely modified to	Highly preferred indications
	test immunomodulatory and	include autoimmune diseases
-	diffferentiation activity of	(e.g., rheumatoid arthritis,
	polypeptides of the invention	systemic lupus erythematosis,
	(including antibodies and	multiple sclerosis and/or as
	agonists or antagonists of the	described below) and
	invention) include assays	ss (
	disclosed in Miraglia et al., J	described below). Preferred
	Biomolecular Screening 4:193-	indications also include
	204(1999); Rowland et al.,	anemia, pancytopenia,
	"Lymphocytes: a practical	leukopenia, thrombocytopenia,
	approach" Chapter 6:138-160	Hodgkin's disease, acute
-	(2000); Satthaporn and	lymphocytic anemia (ALL),
	Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
-	45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
	158:2919-2925 (1997), the	disease, inflammatory bowel

				contents of each of which are	disease, sepsis, neutropenia,
				herein incorporated by	neutrophilla, psoriasis,
_				reference in its entirety.	suppression of immune
				Human dendritic cells that may	reactions to transplanted
				be used according to these	organs and tissues,
		-		assays may be isolated using	hemophilia, hypercoagulation,
				techniques disclosed herein or	diabetes mellitus, endocarditis,
				otherwise known in the art.	meningitis (bacterial and
				Human dendritic cells are	viral), Lyme Disease, asthma,
				antigen presenting cells in	and allergy Preferred
				suspension culture, which,	indications also include
				when activated by antigen	neoplastic diseases (e.g.,
				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
				and functional activities.	"Hyperproliferative
					Disorders"). Highly preferred
					indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HNGND37	740	Regulation of	Assays for the regulation of	A highly preferred
	_		transcription	transcription through the	indication is diabetes mellitus.
			through the PEPCK	PEPCK promoter are well-	An additional highly preferred

 is herein incorporated by	neuropathy, vision impairment
reference in its entirety.	(e.g., diabetic retinopathy and
Hepatocyte cells that may be	blindness), ulcers and impaired
 used according to these assays	wound healing, infection (e.g.,
are publicly available (e.g.,	an infectious diseases or
through the ATCC) and/or	disorders as described in the
may be routinely generated.	"Infectious Diseases" section
Exemplary liver hepatoma	below, especially of the
cells that may be used	urinary tract and skin), carpal
according to these assays	tunnel syndrome and
include H4lle cells, which	Dupuytren's contracture).
contain a tyrosine amino	An additional highly preferred
 transferase that is inducible	indication is obesity and/or
with glucocorticoids, insulin,	complications associated with
 or cAMP derivatives.	obesity. Additional highly
	preferred indications include
	weight loss or alternatively,
	weight gain. Additional
	highly preferred indications are
	complications associated with
	insulin resistance.
	Additional highly preferred
	indications are disorders of the
	musculoskeletal systems
	including myopathies,
	muscular dystrophy, and/or as
	described herein.
	Additional highly preferred
	indications include glycogen
	storage disease (e.g.,
	glycogenoses), hepatitis,

			gallstones, cirrhosis of the
			liver, degenerative or necrotic
а,			liver disease, alcoholic liver
			diseases, fibrosis, liver
			regeneration, metabolic
	-		disease, dyslipidemia and
	_		cholesterol metabolism, and
			hepatocarcinomas.
			Highly preferred indications
-			include blood disorders (e.g.,
			as described below under
			"Immune Activity",
			"Cardiovascular Disorders",
		•	and/or "Blood-Related
			Disorders"), immune disorders
			(e.g., as described below under
			"Immune Activity"), infection
	-		(e.g., an infectious disease
			and/or disorder as described
			below under "Infectious
			Disease"), endocrine disorders
			(e.g., as described below under
			"Endocrine Disorders"), and
			neural disorders (e.g., as
			described below under "Neural
			Activity and Neurological
			Diseases").
			Additional preferred
			indications include neoplastic
			diseases (e.g., as described
			helow under

"Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel
	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium.
	Stimulation of Calcium Flux in pancreatic beta cells.
	741
	HNGOI12

an in	an influx of calcium, leading to	blockage, heart disease, stroke,
activ		impotence (e.g., due to diabetic
respo	responsive signaling pathways	neuropathy or blood vessel
and a	and alterations in cell	blockage), seizures, mental
funct	functions. Exemplary assays	confusion, drowsiness,
that r	that may be used or routinely	nonketotic hyperglycemic-
ipom	modified to measure calcium	hyperosmolar coma,
l flux	flux by polypeptides of the	cardiovascular disease (e.g.,
inver	invention (including antibodies	heart disease, atherosclerosis,
anda	and agonists or antagonists of	microvascular disease,
the ir	the invention) include assays	hypertension, stroke, and other
discl	disclosed in: Satin LS, et al.,	diseases and disorders as
Endo	Endocrinology, 136(10):4589-	described in the
(901)	601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
Endo	Endocrinology, 136(7):2960-6	section below), dyslipidemia,
(1993)	(1995); Richardson SB, et al.,	endocrine disorders (as
Bioc	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
(1992)	(1992); and, Meats, JE, et al.,	Disorders" section below),
Cell	Cell Calcium 1989 Nov-	neuropathy, vision impairment
Dec:	Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
conte	contents of each of which is	blindness), ulcers and impaired
herei	herein incorporated by	wound healing, and infection
refer	reference in its entirety.	(e.g., infectious diseases and
Panc	Pancreatic cells that may be	disorders as described in the
pesn	used according to these assays	"Infectious Diseases" section
are p	are publicly available (e.g.,	below, especially of the
thron	through the ATCC) and/or	urinary tract and skin), carpal
may	may be routinely generated.	tunnel syndrome and
Exen		Dupuytren's contracture).
may	ě	An additional highly preferred
assay	assays include HITT15 Cells.	indication is obesity and/or

			HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HNGOI12	741	Production of IL-10 and activation of T-cells.	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as

described below), boosting a T	cell-mediated immune	response, and suppressing a 1	cell-mediated immune	response.																										
polypeptides and antibodies of	the invention (including	agonists of antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete	IL4, IL10, IL13, IL5 and IL6.	Factors that induce	differentiation and activation	of Th2 cells play a major role	in the initiation and
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						-																								

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boosting a T cell-mediated immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia.
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety.	Human T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the JURKAT	cell line, which is a suspension	culture of leukemia cells that	produce IL-2 when stimulated.									
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				metaplasia, and/or dysplasia.
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
		•		reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HNGOU56	743	Protection from	Caspase Apoptosis Rescue.	A highly preferred
		Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
		Apoptosis.	rescue are well known in the	includes a method for
			art and may be used or	stimulating endothelial cell
			routinely modified to assess	growth. An alternative highly
			the ability of the polypeptides	preferred embodiment of the
			of the invention (including	invention includes a method

		antihodies and agonists or	for inhibiting endothelial cell
		antagonists of the invention) to	growth. A highly preferred
		inhibit caspase protease-	O)
		mediated apoptosis.	includes a method for
		Exemplary assays for caspase	stimulating endothelial cell
		apoptosis that may be used or	proliferation. An alternative
		 routinely modified to test	highly preferred embodiment
		 caspase apoptosis rescue of	of the invention includes a
		polypeptides of the invention	method for inhibiting
		 (including antibodies and	endothelial cell proliferation.
		 agonists or antagonists of the	A highly preferred
		 invention) include the assays	embodiment of the invention
		disclosed in Romeo et al.,	includes a method for
		Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
·		(2000); Messmer et al., Br J	growth. An alternative highly
		 Pharmacol 127(7): 1633-1640	preferred embodiment of the
		 (1999); and J Atheroscler	invention includes a method
	*****	Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
		the contents of each of which	growth. A highly preferred
		 are herein incorporated by	embodiment of the invention
		 reference in its entirety.	includes a method for
		Endothelial cells that may be	stimulating apoptosis of
		used according to these assays	endothelial cells. An
		are publicly available (e.g.,	alternative highly preferred
		through commercial sources).	embodiment of the invention
		Exemplary endothelial cells	includes a method for
		 that may be used according to	inhibiting (e.g., decreasing)
		 these assays include bovine	apoptosis of endothelial cells.
		aortic endothelial cells	A highly preferred
		(bAEC), which are an example	embodiment of the invention
		of endothelial cells which line	includes a method for

	blood vessels and are involved in functions that include, but	stimulating angiogenisis. An alternative highly preferred
	are not limited to, angiogenesis, vascular	embodiment of the invention includes a method for
	permeability, vascular tone,	inhibiting angiogenesis. A
	and immune cell extravasation.	highly preferred embodiment
		method for reducing cardiac
		hypertrophy. An alternative
*		highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
•		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under
		.'Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,
		intracardiac shunt, cardiac
		hypertrophy, myocardial
		infarction, chronic
		hemodynamic overload, and/or

"Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels
themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications
include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma,

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angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	asc	and cancer. Highly
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_	 include trauma such as
	 wounds, burns, and injured
	tissue (e.g., vascular injury
	such as, injury resulting from
	 balloon angioplasty, and
	 atheroschlerotic lesions),
	implant fixation, scarring,
	 ischemia reperfusion injury,
	rheumatoid arthritis,
	 cerebrovascular disease, renal
	diseases such as acute renal
	 failure, and osteoporosis.
	 Additional highly preferred
	 indications include stroke,
	 graft rejection, diabetic or
	 other retinopathies, thrombotic
	 and coagulative disorders,
	vascularitis, lymph
	angiogenesis, sexual disorders,
	 age-related macular
	degeneration, and treatment
	/prevention of endometriosis
	 and related conditions.
	Additional highly preferred
	 indications include fibromas,
	 heart disease, cardiac arrest,
	 heart valve disease, and
	 vascular disease. Preferred
	indications include blood
	disorders (e.g., as described

				below under "Immune
				Activity", "Blood-Related
				Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
	,			inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HNGOW62	744	Protection from	Caspase Apoptosis Rescue.	A highly preferred
		Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
		Apoptosis.	rescue are well known in the	includes a method for
			art and may be used or	stimulating endothelial cell
			routinely modified to assess	growth. An alternative highly
			the ability of the polypeptides	preferred embodiment of the
			of the invention (including	invention includes a method
			antibodies and agonists or	for inhibiting endothelial cell
			antagonists of the invention) to	growth. A highly preferred
			inhibit caspase protease-	embodiment of the invention
			mediated apoptosis.	includes a method for

stimulating endothelial cell proliferation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting	endothelial cell proliferation.	A highly preferred embodiment of the invention	includes a method for	stimulating endothelial cell	growth. An alternative highly	preferred embodiment of the	invention includes a method	~~	growth. A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for
Exemplary assays for caspase apoptosis that may be used or routinely modified to test	caspase apoptosis rescue of	(including antibodies and	agonists or antagonists of the	disclosed in Romeo et al.,	Cardiovasc Res 45(3): 788-794	(2000); Messmer et al., Br J	Pharmacol 127(7): 1633-1640	(1999); and J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis vascular
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	permeability, vascular tone.	inhibiting angiogenesis. A
	and immune cell extravasation.	men
		of the invention includes a
		method for reducing cardiac
		hypertrophy. An alternative
		highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
· · · · ·		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under
 		"Hyperproliferative
		Disorders"), and disorders of
 		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
 		aortic stenosis,
 		cardiomyopathy, valvular
 		regurgitation, left ventricular
 		dysfunction, atherosclerosis
 		and atherosclerotic vascular
		disease, diabetic nephropathy,
		intracardiac shunt, cardiac
		hypertrophy, myocardial
 		infarction, chronic
		hemodynamic overload, and/or
		as described below under
		"Cardiovascular Disorders").
		Highly preferred indications
		include cardiovascular,

			endothelial and/or angiogenic
			disorders (e.g., systemic
			disorders that affect vessels
			such as diabetes mellitus, as
			well as diseases of the vessels
		-	themselves, such as of the
		-	arteries, capillaries, veins
-			and/or lymphatics). Highly
			preferred are indications that
			stimulate angiogenesis and/or
		-	cardiovascularization. Highly
			preferred are indications that
			inhibit angiogenesis and/or
			cardiovascularization.
			Highly preferred indications
			include antiangiogenic activity
			to treat solid tumors,
			leukemias, and Kaposi"s
		-	sarcoma, and retinal disorders.
		-	Highly preferred indications
			include neoplasms and cancer,
			such as, Kaposi"s sarcoma,
			hemangioma (capillary and
			cavernous), glomus tumors,
			telangiectasia, bacillary
			angiomatosis,
			hemangioendothelioma,
			angiosarcoma,
			haemangiopericytoma,
			lymphangioma,
			lymphangiosarcoma. Highly

preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury
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 		such balle	such as, injury resulting from balloon angioplasty, and
 		athe	atheroschlerotic lesions), implant fixation, scarring.
	_	isch	ischemia reperfusion injury,
 		rhen	rheumatoid arthritis,
 		cere	cerebrovascular disease, renal
		dise	diseases such as acute renal
	· <u> </u>	failu	failure, and osteoporosis.
		Add	Additional highly preferred
 		ipui	indications include stroke,
		graf	graft rejection, diabetic or
		othe	other retinopathies, thrombotic
		and	and coagulative disorders,
		vasc	vascularitis, lymph
	-	angi	angiogenesis, sexual disorders,
		age-	age-related macular
 		geb	degeneration, and treatment
		/pre	/prevention of endometriosis
 		and	and related conditions.
 		Add	Additional highly preferred
 -		ipui	indications include fibromas,
 		hear	heart disease, cardiac arrest,
 		hear	heart valve disease, and
 -		vasc	vascular disease. Preferred
		ipui	indications include blood
		diso	disorders (e.g., as described
 		belo	below under "Immune
		Acti	Activity", "Blood-Related
		Disc	Disorders", and/or
		ري الم	"Cardiovascular Disordere")

				Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain
нине из	745	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders",

			vessels, and are involved in	"Hyperproliferative Disorders"
			functions that include, but are	and/or "Cardiovascular
			not limited to, angiogenesis,	Disorders"). Highly preferred
-			vascular permeability, vascular	indications include neoplasms
			tone, and immune cell	and cancers such as, for
			extravasation. Exemplary	example, leukemia, lymphoma,
			endothelial cells that may be	melanoma, renal cell
			used according to these assays	carcinoma, and prostate,
			include human umbilical vein	breast, lung, colon, pancreatic,
			endothelial cells (HUVEC),	esophageal, stomach, brain,
			which are available from	liver and urinary cancer. Other
			commercial sources. The	preferred indications include
			expression of VCAM	benign dysproliferative
			(CD106), a membrane-	disorders and pre-neoplastic
			associated protein, can be	conditions, such as, for
			upregulated by cytokines or	example, hyperplasia,
			other factors, and contributes	metaplasia, and/or dysplasia.
			to the extravasation of	
 			lymphocytes, leucocytes and	
			other immune cells from blood	
			vessels; thus VCAM	
			expression plays a role in	
			promoting immune and	
			inflammatory responses.	
HNHEU93	745	Stimulation of	Assays for measuring secretion	A highly preferred
		insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
		from pancreatic	the art and may be used or	An additional highly preferred
		beta cells.	routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease

(e.g., renal failure, nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection
antagonists of the invention) to stimulate insulin secretion.	For example, insulin secretion	is measured by FMAT using	anti-rat insulin antibodies.	Insulin secretion from	pancreatic beta cells is	upregulated by glucose and	also by certain	proteins/peptides, and	disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to	test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,	138(9):3735-40 (1997); Kim,	K.H., et al., FEBS Lett,	377(2):237-9 (1995); and,	Miraglia S et. al., Journal of	Biomolecular Screening,	4:193-204 (1999), the contents	of each of which is herein
		-																											-

			incorporated by reference in its entirety. Pancreatic cells that	(e.g., infectious diseases and disorders as described in the
			may be used according to these	"Infectious Diseases" section
			assays are publicly available	below, especially of the
			(e.g., through the ATCC)	urinary tract and skin), carpal
			and/or may be routinely	tunnel syndrome and
			generated. Exemplary	Dupuytren's contracture).
			pancreatic cells that may be	An additional highly preferred
			used according to these assays	indication is obesity and/or
			include rat INS-1 cells. INS-1	complications associated with
 		-	cells are a semi-adherent cell	obesity. Additional highly
			line established from cells	preferred indications include
		~	isolated from an X-ray induced	weight loss or alternatively,
			rat transplantable insulinoma.	weight gain. Aditional
			These cells retain	highly preferred indications are
			characteristics typical of native	complications associated with
			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
			secretion. References: Asfari	
			et al. Endocrinology 1992	
111111111111111111111111111111111111111	110		130:16/.	
 HNHFM14	746	Inhibition of	Reporter Assay: construct	
		squalene synthetase	contains regulatory and coding	
		gene transcription.	sequence of squalene	
			synthetase, the first specific	
 			enzyme in the cholesterol	
			biosynthetic pathway. See	
			Jiang, et al., J. Biol. Chem.	
 			268:12818-128241(993), the	
			contents of which are herein	
	ļ		incorporated by reference in its	

				entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al.,	
				Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	
 	HNHFM14	746	Stimulation of Calcium Flux in	Assays for measuring calcium flux are well-known in the art	A highly preferred indication is diabetes mellitus.
			pancreatic beta	and may be used or routinely	An additional highly preferred
			cells.	modified to assess the ability of polypeptides of the	indication is a complication associated with diabetes (e.g.,
				invention (including antibodies	diabetic retinopathy, diabetic
				and agonists or antagonists of	nephropathy, kidney disease
_				the invention) to mobilize	(e.g., renal failure,
				calcium. For example, the	nephropathy and/or other
				measure influx of calcium.	described in the "Renal
				Cells normally have very low	Disorders" section below),
				concentrations of cytosolic	diabetic neuropathy, nerve
				calcium compared to much	disease and nerve damage
				higher extracellular calcium.	(e.g., due to diabetic
				Extracellular factors can cause	neuropathy), blood vessel
				an influx of calcium, leading to	blockage, heart disease, stroke,
				activation of calcium	impotence (e.g., due to diabetic
				responsive signaling pathways	neuropathy or blood vessel
				and alterations in cell	blockage), seizures, mental

iess,	ycemic-	a,	ease (e.g.,	rosclerosis,	ase,	te, and other	lers as		isorders"	slipidemia,	s (as	Indocrine	below),	impairment	opathy and	and impaired	d infection	seases and	bed in the	es" section	of the	kin), carpal	pu	acture).	ly preferred	ty and/or	ciated with	ıl highly	ns include	
confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	
functions. Exemplary assays c	that may be used or routinely	modified to measure calcium h	flux by polypeptides of the	invention (including antibodies h			disclosed in: Satin LS, et al.,	Endocrinology, 136(10):4589-		~		Biochem J, 288 (Pt 3):847-51 c			Dec;10(8):535-41 (1989), the	contents of each of which is	herein incorporated by	reference in its entirety.	Pancreatic cells that may be	used according to these assays "		through the ATCC) and/or u	may be routinely generated.	that	ė	assays include HITT15 Cells.	HITT15 are an adherent c	epithelial cell line established c	from Syrian hamster islet cells p	
functio	that ma	fipom	flux by	inventi	and ag	the inv	disclos	Endoci	(1)	Endoc	(1995)	Bioche	(1992)	Cell C	Dec;1(conten	herein	referen	Pancre	used a	are put	throug	may be	Exemp	may be	assays	HITTI	epithel	S morf	
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			cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or	weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
			glucocorticolds. At 1 C# CKL-177 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
HNHNB29	748	Regulation of transcription through the PFPCK	Assays for the regulation of transcription through the PFPCK promoter are well-	A highly preferred indication is diabetes mellitus.
		promoter in hepatocytes	known in the art and may be used or routinely modified to	indication is a complication associated with diabetes (e.g.,
			assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	naperic reinopainy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other
			invention) to activate the PEPCK promoter in a reporter construct and regulate liver gluconeogenesis. Exemplary	diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve
			assays for regulation of transcription through the PEPCK promoter that may be	disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel
			used or routinely modified to test for PEPCK promoter	blockage, heart disease, stroke, impotence (e.g., due to diabetic

activity (in hepatocytes) of	tes) of	neuropathy or blood vessel
 polypeptides of the invention	nvention	blockage), seizures, mental
 (including antibodies and	s and	confusion, drowsiness,
 agonists or antagonists of the	sts of the	nonketotic hyperglycemic-
 invention) include assays	ssays	hyperosmolar coma,
disclosed in Berger et al., Gene	et al., Gene	cardiovascular disease (e.g.,
 66:1-10 (1998); Cullen and	len and	heart disease, atherosclerosis,
 Malm, Methods in Enzymol	Snzymol	microvascular disease,
 216:362-368 (1992); Henthorn	; Henthorn	hypertension, stroke, and other
 et al., Proc Natl Acad Sci USA	d Sci USA	diseases and disorders as
85:6342-6346 (1988);	··	described in the
 Lochhead et al., Diabetes	betes	"Cardiovascular Disorders"
49(6):896-903 (2000); and)); and	section below), dyslipidemia,
Yeagley et al., J Biol Chem	l Chem	endocrine disorders (as
 275(23):17814-17820 (2000),	20 (2000),	described in the "Endocrine
the contents of each of which	of which	Disorders" section below),
is herein incorporated by	d by	neuropathy, vision impairment
reference in its entirety.	ety.	(e.g., diabetic retinopathy and
 Hepatocyte cells that may be	t may be	blindness), ulcers and impaired
 used according to these assays	ese assays	wound healing, infection (e.g.,
are publicly available (e.g.,	e (e.g.,	an infectious diseases or
through the ATCC) and/or	and/or	disorders as described in the
may be routinely generated.	nerated.	"Infectious Diseases" section
Exemplary liver hepatoma	atoma	below, especially of the
cells that may be used	pa	urinary tract and skin), carpal
 according to these assays	ssays	tunnel syndrome and
 include H4lle cells, which	which	Dupuytren's contracture).
 contain a tyrosine amino	nino	An additional highly preferred
 transferase that is inducible	ducible	indication is obesity and/or
with glucocorticoids, insulin,	, insulin,	complications associated with
or cAMP derivatives.	S.	obesity. Additional highly

preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include glycogen	storage disease (e.g.,	glycogenoses), hepatitis,	gallstones, cirrhosis of the	liver, degenerative or necrotic	liver disease, alcoholic liver	diseases, fibrosis, liver	regeneration, metabolic	disease, dyslipidemia and	cholesterol metabolism, and	hepatocarcinomas.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders" immine disorders
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						_	-																							

'Immune Activity', infection (**e., an infectious disease and/or disorder as described below under "Infectious Disease"), endocrine disorders (*e., as described below under "Endocrine Disorders'), and neural disorders (*e., as described below under "Neural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplastic, sosophageal, stomach, brain, and uninary cancer. A highly preferred unidication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasta, and/or dysplasia.	(e a se described below under
(e.g., an infectious disease and/or disorder as described below under "infectious disease") and pelos with "infectious Disease"), endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neural disorders (e.g., as described below under "Yeural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperpolificative Disorders"). Preferred indications include neoplastic diseases (e.g., as described below under "Hyperpolificative Disorders"). Preferred indications include heoplasms, hymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and unimary cancer. A highly preferred indications include benigm dysproliferative disorders and pre-reoplastic conditions, such as, for example, hyperplasia, metaplasia, and or dysprolasia, and or dysprolasia, and or dysprolasia, and dy or dysplasia.	
andor disorder as described below under "Infectious below under "Infectious below under "Infectious blook and "Endocrine disorders (e.g., as described below under "Neural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Neural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperpoliferative Disorders"). Preferred indications include neoplastic diseases (e.g., as described below under "Hyperpoliferative Disorders"). Preferred indications include benign dayproliferative disorders and urinary cancer. A highly preferred indication is liver cancer, other preferred indications include benign dysproliferative disorders and pre-reoplastic conditions, such as, for example, hyperplasia, metaplasia, andor dysplasia.	Immune Activity), infection
pandor disorder as described below under "Infections Disease"), endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neutral disorders (e.g., as described below under "Neural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplastic diseases (e.g., as described indications include neoplastic cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic outditions, such as, for example, hyperpalasia, metaplastia, andor dysplasia.	(e.g., an infectious disease
Disease"), and orderine disorders (e.g., as described below under "Endocrine Disorders"), and neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperprofiferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and unitary cancer. A highly preferred indication is ilver cancer. Other preferred indications include benign dysprofiferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	and/or disorder as described
Disease"), endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and uninary cancer. A highly preferred indication is include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, and/or dysplasia, metaplasia, and/or dysplasia.	below under "Infectious
(e.g., as described below under "Endocrine Disorders"), and neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, prain, and uninary cancer. A highly preferred indications include benign dysproliferative disorders and prepropliative disorders and preproplative disorders and preproplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Disease"), endocrine disorde
"Endocrine Disorders"), and neural disorders (e.g., as described below under "Neural Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostace, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	(e.g., as described below und
described below under "Neural Activity and Neurological Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperpoliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and uninary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	 "Endocrine Disorders"), and
described below under "Neural Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	neural disorders (e.g., as
Activity and Neurological Diseases"). Additional preferred indications include reoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia. metaplasia, and/or dysplasia.	 described below under "Neu
Diseases"). Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperpolitierative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and dysproliferative disorders and dysproliferative disorders and dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia.	Activity and Neurological
Additional preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia.	Diseases").
indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Additional preferred
diseases (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	indications include neoplasti
below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	diseases (e.g., as described
"Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	below under
Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	"Hyperproliferative
indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Disorders"). Preferred
and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	indications include neoplasn
lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	and cancers, such as, leuken
lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	lymphoma, prostate, breast,
esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	lung, colon, pancreatic,
and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	esophageal, stomach, brain,
preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	and urinary cancer. A highly
cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	preferred indication is liver
indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	cancer. Other preferred
dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	indications include benign
pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	dysproliferative disorders an
as, for example, hyperplasia, metaplasia, and/or dysplasia.	pre-neoplastic conditions, su
metaplasia, and/or dysplasia.	as, for example, hyperplasia
	metaplasia, and/or dysplasia

HNHOD46	16 749	SEAP in 293/ISRE		
7OHNH		Activation of	Kinase assay. Kinase assays,	A highly preferred
		Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
		Signaling Pathway	assay, for ERK signal	includes a method for
			transduction that regulate cell	stimulating adipocyte
		-	proliferation or differentiation	proliferation. An alternative
			are well known in the art and	highly preferred embodiment
			may be used or routinely	of the invention includes a
			modified to assess the ability	method for inhibiting
			of polypeptides of the	adipocyte proliferation. A
			invention (including antibodies	highly preferred embodiment
			and agonists or antagonists of	of the invention includes a
			the invention) to promote or	method for stimulating
	<u> </u>		inhibit cell proliferation,	adipocyte differentiation. An
			activation, and differentiation.	alternative highly preferred
			Exemplary assays for ERK	embodiment of the invention
			kinase activity that may be	includes a method for
			used or routinely modified to	inhibiting adipocyte
		•	test ERK kinase-induced	differentiation. A highly
	_		activity of polypeptides of the	preferred embodiment of the
	_		invention (including antibodies	invention includes a method
	_		and agonists or antagonists of	for stimulating (e.g.,
			the invention) include the	increasing) adipocyte
			assays disclosed in Forrer et	activation. An alternative
			al., Biol Chem 379(8-9):1101-	highly preferred embodiment
			1110 (1998); Le Marchand-	of the invention includes a
			Brustel Y, Exp Clin	method for inhibiting the
			Endocrinol Diabetes	activation of (e.g., decreasing)
			107(2):126-132 (1999);	and/or inactivating adipocytes.
			Kyriakis JM, Biochem Soc	Highly preferred indications
			Symp 64:29-48 (1999); Chang	include endocrine disorders

		and Karin, Nature 410(6824):37-40 (2001); and	(e.g., as described below under "Endocrine Disorders").
		Cobb MH, Prog Biophys Mol	Highly preferred indications
		Biol 71(3-4):479-500 (1999);	also include neoplastic
		the contents of each of which	diseases (e.g., lipomas,
		are herein incorporated by	liposarcomas, and/or as
		reference in its entirety.	described below under
		Mouse adipocyte cells that	"Hyperproliferative
		may be used according to these	Disorders"). Preferred
		assays are publicly available	indications include blood
		(e.g., through the ATCC).	disorders (e.g., hypertension,
		Exemplary mouse adipocyte	congestive heart failure, blood
		cells that may be used	vessel blockage, heart disease,
		according to these assays	stroke, impotence and/or as
		include 3T3-L1 cells. 3T3-L1	described below under
		is an adherent mouse	"Immune Activity",
	-	preadipocyte cell line that is a	"Cardiovascular Disorders",
		continuous substrain of 3T3	and/or "Blood-Related
		fibroblast cells developed	Disorders"), immune disorders
		through clonal isolation and	(e.g., as described below under
		undergo a pre-adipocyte to	"Immune Activity"), neural
		adipose-like conversion under	disorders (e.g., as described
•		appropriate differentiation	below under "Neural Activity
•		conditions known in the art.	and Neurological Diseases"),
			and infection (e.g., as
			described below under
•			"Infectious Disease").
			A highly preferred indication
			is diabetes mellitus. An
			additional highly preferred
<u>.</u>			indication is a complication

		associated with diahetes (e a
 -		diahetic retinonathy diahetic
 		diabetic reminipanity, diabetic
 		nephropathy, kidney disease
 		(e.g., renal failure,
 		nephropathy and/or other
 		diseases and disorders as
 		described in the "Renal
		Disorders" section below),
		diabetic neuropathy, nerve
-		disease and nerve damage
		(e.g., due to diabetic
		neuropathy), blood vessel
-		blockage, heart disease, stroke,
	_	impotence (e.g., due to diabetic
		neuropathy or blood vessel
		blockage), seizures, mental
		confusion, drowsiness,
		nonketotic hyperglycemic-
		hyperosmolar coma,
 		cardiovascular disease (e.g.,
		heart disease, atherosclerosis,
		microvascular disease,
		hypertension, stroke, and other
		diseases and disorders as
		described in the
		"Cardiovascular Disorders"
		section below), dyslipidemia,
 		endocrine disorders (as
		described in the "Endocrine
		Disorders" section below),
		neuropathy, vision impairment

(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,
					-																							-		

				and kidney diseases or
				disorders. Preferred
				indications include neoplasms
				and cancer, such as,
				lymphoma, leukemia and
				breast, colon, and kidney
				cancer. Additional preferred
				indications include melanoma,
				prostate, lung, pancreatic,
				esophageal, stomach, brain,
				liver, and urinary cancer.
				Highly preferred indications
				include lipomas and
				liposarcomas. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
				as, for example, hyperplasia,
				metaplasia, and/or dysplasia.
HNHOD46	749	Regulation of	Assays for the regulation of	A highly preferred indication
		transcription via	transcription through the	is diabetes mellitus.
		DMEF1 response	DMEF1 response element are	Additional highly preferred
		element in	well-known in the art and may	indications include
		adipocytes and pre-	be used or routinely modified	complications associated with
		adipocytes	to assess the ability of	diabetes (e.g., diabetic
			polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to activate the	nephropathy and/or other
			DMEF1 response element in a	diseases and disorders as
			reporter construct (such as that	described in the "Renal

containing the GLUT4 promoter) and to regulate insulin production. The DMEFI response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another required for insulin regulation of Glut4 expression in skeletal muscle GLUT4 is the primary of Glut4 expression in skeletal insulin-responsive glucose transporter in fat and muscle transp	s f
containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed inThai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 20(45):28514-21 (1994); "Identification of a 30- base pair regulatory element	containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention including antibodies and agonists or antagonists of the invention) include assays disclosed inThai, M.V., et al., J Biol Chem, 273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30- base pair regulatory element

			protein that regulates the	urinary tract and skin). An additional highly preferred
			transgenic mice", J Biol Chem.	indication is obesity and/or
			2000 Aug 4;275(31):23666-73;	complications associated with
			Berger, et al., Gene 66:1-10	obesity. Additional highly
			(1988); and, Cullen, B., et al.,	preferred indications include
-			Methods in Enzymol.	weight loss or alternatively,
			216:362–368 (1992), the	weight gain. Additional highly
			contents of each of which is	preferred indications are
			herein incorporated by	complications associated with
_			reference in its entirety.	insulin resistance.
-			Adipocytes and pre-adipocytes	
			that may be used according to	
			these assays are publicly	
			available (e.g., through the	-
			ATCC) and/or may be	
			routinely generated.	
			Exemplary cells that may be	-
			used according to these assays	
			include the mouse 3T3-L1 cell	
			line which is an adherent	
			mouse preadipocyte cell line.	
			Mouse 3T3-L1 cells are a	
			continuous substrain of 3T3	
			fibroblasts developed through	
			clonal isolation. These cells	
			undergo a pre-adipocyte to	
			adipose-like conversion under	
	_		appropriate differentiation	
			culture conditions.	
HNHOD46	749	Activation of	Assays for the activation of	A highly preferred indication

transcription	transcription through the	is obesity and/or complications
through cAMP	cAMP response element are	associated with obesity.
response element	well-known in the art and may	Additional highly preferred
 (CRE) in pre-	be used or routinely modified	indications include weight loss
 adipocytes.	to assess the ability of	or alternatively, weight gain.
	polypeptides of the invention	An additional highly preferred
	(including antibodies and	indication is diabetes mellitus.
	agonists or antagonists of the	An additional highly preferred
	invention) to increase cAMP,	indication is a complication
	regulate CREB transcription	associated with diabetes (e.g.,
	factors, and modulate	diabetic retinopathy, diabetic
	expression of genes involved	nephropathy, kidney disease
	in a wide variety of cell	(e.g., renal failure,
	functions. For example, a	nephropathy and/or other
	3T3-L1/CRE reporter assay	diseases and disorders as
	may be used to identify factors	described in the "Renal
	that activate the cAMP	Disorders" section below),
	signaling pathway. CREB	diabetic neuropathy, nerve
	plays a major role in	disease and nerve damage
	adipogenesis, and is involved	(e.g., due to diabetic
	in differentiation into	neuropathy), blood vessel
	adipocytes. CRE contains the	blockage, heart disease, stroke,
	binding sequence for the	impotence (e.g., due to diabetic
	transcription factor CREB	neuropathy or blood vessel
	(CRE binding protein).	blockage), seizures, mental
	Exemplary assays for	confusion, drowsiness,
 	transcription through the	nonketotic hyperglycemic-
	cAMP response element that	hyperosmolar coma,
	may be used or routinely	cardiovascular disease (e.g.,
 	modified to test cAMP-	heart disease, atherosclerosis,
	response element activity of	microvascular disease,

		polypeptides of the invention	hypertension, stroke, and other
		(including antibodies and	diseases and disorders as
		agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
		disclosed in Berger et al., Gene	section below), dyslipidemia,
		66:1-10 (1998); Cullen and	endocrine disorders (as
		Malm, Methods in Enzymol	described in the "Endocrine
		216:362-368 (1992); Henthorn	Disorders" section below),
		et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	-	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
		et al., Mol Cell Biol	blindness), ulcers and impaired
		20(3):1008-1020 (2000); and	wound healing, and infection
		Klemm et al., J Biol Chem	(e.g., infectious diseases and
	-	273:917-923 (1998), the	disorders as described in the
		contents of each of which are	"Infectious Diseases" section
	-	herein incorporated by	below, especially of the
		reference in its entirety. Pre-	urinary tract and skin), carpal
		adipocytes that may be used	tunnel syndrome and
		according to these assays are	Dupuytren's contracture).
-		publicly available (e.g.,	Additional highly preferred
		through the ATCC) and/or	indications are complications
		may be routinely generated.	associated with insulin
		Exemplary mouse adipocyte	resistance.
		cells that may be used	
		according to these assays	
		include 3T3-L1 cells. 3T3-L1	
		is an adherent mouse	
		preadipocyte cell line that is a	
	-	continuous substrain of 3T3	
		fibroblast cells developed	
		through clonal isolation and	

				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
	HNHOD46	749	Activation of	Assays for the activation of	A highly preferred indication
			transcription	transcription through the	is obesity and/or complications
			through serum	Serum Response Element	associated with obesity.
			response element in	(SRE) are well-known in the	Additional highly preferred
			pre-adipocytes.	art and may be used or	indications include weight loss
				routinely modified to assess	or alternatively, weight gain.
				the ability of polypeptides of	An additional highly preferred
				the invention (including	indication is diabetes mellitus.
				antibodies and agonists or	An additional highly preferred
				antagonists of the invention) to	indication is a complication
				regulate the serum response	associated with diabetes (e.g.,
				factors and modulate the	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in growth. Exemplary assays	(e.g., renal failure,
				for transcription through the	nephropathy and/or other
				SRE that may be used or	diseases and disorders as
				routinely modified to test SRE	described in the "Renal
				activity of the polypeptides of	Disorders" section below),
				the invention (including	diabetic neuropathy, nerve
				antibodies and agonists or	disease and nerve damage
				antagonists of the invention)	(e.g., due to diabetic
-				include assays disclosed in	neuropathy), blood vessel
		*		Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
				(1998); Cullen and Malm,	impotence (e.g., due to diabetic
				Methods in Enzymol 216:362-	neuropathy or blood vessel
				368 (1992); Henthorn et al.,	blockage), seizures, mental
				Proc Natl Acad Sci USA	confusion, drowsiness,

			85:6342-6346 (1988); and	nonketotic hyperglycemic-
			Black et al., Virus Genes	hyperosmolar coma,
			12(2):105-117 (1997), the	cardiovascular disease (e.g.,
			content of each of which are	heart disease, atherosclerosis,
			herein incorporated by	microvascular disease,
			reference in its entirety. Pre-	hypertension, stroke, and other
			adipocytes that may be used	diseases and disorders as
			according to these assays are	described in the
			publicly available (e.g.,	"Cardiovascular Disorders"
			through the ATCC) and/or	section below), dyslipidemia,
			may be routinely generated.	endocrine disorders (as
			Exemplary mouse adipocyte	described in the "Endocrine
			cells that may be used	Disorders" section below),
			according to these assays	neuropathy, vision impairment
			include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
			is an adherent mouse	blindness), ulcers and impaired
			preadipocyte cell line that is a	wound healing, and infection
			continuous substrain of 3T3	(e.g., infectious diseases and
			fibroblast cells developed	disorders as described in the
			through clonal isolation and	"Infectious Diseases" section
			undergo a pre-adipocyte to	below). Additional highly
			adipose-like conversion under	preferred indications are
			appropriate differentiation	complications associated with
			conditions known in the art.	insulin resistance.
HNHOD46	749	Activation of	Assays for the activation of	Preferred indications include
		transcription	transcription through the	blood disorders (e.g., as
		through cAMP	cAMP response element are	described below under
		response element in	well-known in the art and may	"Immune Activity", "Blood-
		immune cells (such	be used or routinely modified	Related Disorders", and/or
		as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
			polypeptides of the invention	and infection (e.g., an

infectious disease as described	below under "Infectious	Disease"). Preferred	indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma	(e.g., T cell lymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin's disease),	melanoma, and prostate,
(including antibodies and	agonists or antagonists of the	invention) to increase cAMP	and regulate CREB	transcription factors, and	modulate expression of genes	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the cAMP response	element that may be used or	routinely modified to test	cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are
										-																				
																								<u> </u>			• • •			

				publicly available (e.g., through the ATCC).	breast, lung, colon, pancreatic, esophageal, stomach, brain,
				Exemplary mouse T cells that	liver and urinary cancer. Other
				may be used according to these assays include the CTLL cell	preferred indications include benign dysproliferative
				line, which is a suspension	disorders and pre-neoplastic
				culture of IL-2 dependent	conditions, such as, for
				cytotoxic T cells.	example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
	-				multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HNHOD46	749	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
-					

	as T-cells).	routinely modified to assess	preferred embodiment of the	
		the ability of polypeptides of	invention includes a method	
		the invention (including	for stimulating (e.g.,	_
		antibodies and agonists or	increasing) TNF alpha	
		antagonists of the invention) to	production. Preferred	
		regulate the serum response	indications include blood	
		factors and modulate the	disorders (e.g., as described	
		expression of genes involved	below under "Immune	
		in growth. Exemplary assays	Activity", "Blood-Related	
_		for transcription through the	Disorders", and/or	
		SRE that may be used or	"Cardiovascular Disorders"),	
		routinely modified to test SRE	Highly preferred indications	
		activity of the polypeptides of	include autoimmune diseases	
		the invention (including	(e.g., rheumatoid arthritis,	
		antibodies and agonists or	systemic lupus erythematosis,	
		antagonists of the invention)	Crohn"s disease, multiple	
		include assays disclosed in	sclerosis and/or as described	
		Berger et al., Gene 66:1-10	below), immunodeficiencies	
		(1998); Cullen and Malm,	(e.g., as described below),	
		Methods in Enzymol 216:362-	boosting a T cell-mediated	
		368 (1992); Henthorn et al.,	immune response, and	
		Proc Natl Acad Sci USA	suppressing a T cell-mediated	
		85:6342-6346 (1988); and	immune response. Additional	
		Black et al., Virus Genes	highly preferred indications	
		12(2):105-117 (1997), the	include inflammation and	
		content of each of which are	inflammatory disorders, and	
		herein incorporated by	treating joint damage in	
		reference in its entirety. T	patients with rheumatoid	
		cells that may be used	arthritis. An additional highly	
		according to these assays are	preferred indication is sepsis.	
		publicly available (e.g.,	Highly preferred indications	

	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
 	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
 	dependent suspension culture	highly preferred indications
 	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
 		leukemia, lymphoma,
		melanoma, glioma (e.g.,
 		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
 		esophageal, stomach, brain,
 		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
 		conditions, such as, for
 		example, hyperplasia,
		metaplasia, and/or dysplasia.
 		Preferred indications include
		anemia, pancytopenia,
 		leukopenia, thrombocytopenia,
 		Hodgkin's disease, acute
 		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
 		arthritis, AIDS, granulomatous
 		disease, inflammatory bowel
		disease, neutropenia,

					neutrophilia, psoriasis,
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
	_				disease as described below
					under "Infectious Disease").
	HNHOD46	749	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
		-		disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
•				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),

and infection (e.g., as described below under	"Infectious Disease"). Highly preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred
유등	known in the art and may be		tion	(including antibodies and	agonists or antagonists of the			differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and		polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,
																			-					•				

	neopiasms	as, myeloma,	kemia,	oma, and	ng, colon,	geal,	ver and	ner preferred	benign	sorders and	ditions, such	perplasia,	dysplasia.	ns include	nia,	ocytopenia,	, acute	ia (ALL),	, Burkitt's	s, AIDS,	ease,	el disease,	-	asis,	nune	lanted		coagulation,	endocarditis,	me Disease.
	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.
													_		 -			_			g	in	Se	ne	ns		or	he	d.	<u> </u>
	Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.											
111	Lympr	approac	(2000);	Immuno	(1997),	which a	by refer	Human	be used	assays r	techniq	otherwi	Human	antigen	snspens	when ac	and/or c	upregul	and fun			_								
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														-					_											

					indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	HNHOD46	749	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory	A highly preferred embodiment of the invention	
			Ī	proteins produced by activated	includes a method for	
				dendritic cells that upregulate	stimulating MIP1a production.	
				cell chemotaxis are well	embodiment of the invention	
				known in the art and may be	includes a method for	
				used or routinely modified to	uci	
				assess the ability of	MIP1a production. A highly	
				polypeptides of the invention	preferred indication is	
				(including antibodies and	infection (e.g., an infectious	
				agonists or antagonists of the	disease as described below	
				invention) to mediate	under "Infectious Disease").	
				immunomodulation, modulate	Preferred indications include	
-	-			chemotaxis, and modulate T	blood disorders (e.g., as	
				cell differentiation. Exemplary	described below under	
_				assays that test for	"Immune Activity", "Blood-	
_				immunomodulatory proteins	Related Disorders", and/or	
				evaluate the production of	"Cardiovascular Disorders").	
				chemokines, such as	Highly preferred indications	
_				macrophage inflammatory	include autoimmune diseases	
				protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,	
				the activation of	systemic lupus erythematosis,	
				monocytes/macrophages and T	multiple sclerosis and/or as	
				cells. Such assays that may be	described below) and	
				used or routinely modified to	immunodeficiencies (e.g., as	
				test immunomodulatory and	described below). Additional	

			upregulate T cell proliferation and functional activities.	esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for
HNHOD46	749	SEAP in HIB/CRE		example, nyperplasia, metaplasia, and/or dysplasia.
HNHOD46	749	Activation of transcription	This reporter assay measures activation of the GATA-3	Highly preferred indications include allergy, asthma, and
		through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred indications include infection
		immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to cytokine and chemokine	described below under "Infectious Disease"), and
			production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
			through the GATA3 response	Preferred indications also
			element are well-known in the	include blood disorders (e.g.,
			routinely modified to assess	"Immune Activity", "Blood-
			the ability of polypeptides of	Related Disorders", and/or
			the invention (including	"Cardiovascular Disorders").
			antibodies and agonists or	Preferred indications include
			antagonists of the invention) to	autoimmune diseases (e.g.,
		-	regulate GATA3 transcription	rheumatoid arthritis, systemic
			factors and modulate	lupus erythematosis, multiple
			expression of mast cell genes	sclerosis and/or as described
			important for immune response	below) and
			development. Exemplary	immunodeficiencies (e.g., as

assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
 element that may be used or	diseases (e.g., leukemia,
 routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
 activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
 and agonists or antagonists of	urinary tract cancers and/or as
 the invention) include assays	described below under
 disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
 Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
 et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
 et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
 Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
 J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
 Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
[14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
contents of each of which are	lymphoma, arthritis, AIDS,
herein incorporated by	granulomatous disease,
reference in its entirety. Mast	inflammatory bowel disease,
cells that may be used	sepsis, neutropenia,
according to these assays are	neutrophilia, psoriasis,
publicly available (e.g.,	suppression of immune
 through the ATCC).	reactions to transplanted
Exemplary human mast cells	organs and tissues, hemophilia,

				that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
				immature mast cells.	
	HNHOD46	749	Activation of transcription	This reporter assay measures activation of the NFAT	Highly preferred indications include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
,				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as

immunomodulatory functions.	described below). Preferred
Exemplary assays for	indications include neoplastic
 transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
 modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
 polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
 invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
 Malm, Methods in Enzymol	pre-neoplastic conditions, such
 216:362-368 (1992); Henthorn	as, for example, hyperplasia,
 et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	Preferred indications include
 et al., Int J Biochem Cell Biol	anemia, pancytopenia,
 31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
 et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
 Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
 16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
 al., J Exp Med 188:527-537	granulomatous disease,
 (1998), the contents of each of	inflammatory bowel disease,
 which are herein incorporated	sepsis, neutropenia,
 by reference in its entirety.	neutrophilia, psoriasis,
Mast cells that may be used	suppression of immune
 according to these assays are	reactions to transplanted
publicly available (e.g.,	organs and tissues, hemophilia,

hypercoagulation, diabetes ast cells mellitus, endocarditis, ording to meningitis, and Lyme Disease. the HMC- an st cell line peripheral th mast thibits of	ttion (i.e. ss) of ation of l-known in sed or sasses otides of ing sts or vention) to l dipose For er-Gloô ability p., can be number of e based on TP
through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Proliferation of pre- adipose cells (such increases or decreases) of cells in viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP
	HNHOD46 749 Pr as as
	HZH

				present which signals the	
				presence of metabolically	
				active cells. 3T3-L1 is a	
				mouse preadipocyte cell line. It	
			,	is a continuous substrain of	
				3T3 fibroblast cells developed	
				through clonal isolation. Cells	
				were differentiated to an	
				adipose-like state before being	
				used in the screen. See Green	
				H and Meuth M., Cell 3: 127-	
				133 (1974), which is herein	
				incorporated by reference in its	
				entirety.	
	HNHOD46	749	IL-10 in Human T-		
			cell 2B9		
	HNHOD46	749	SEAP in Jurkat-		
			AP1		
	HNHOD46	749	Activation of	Assays for the activation of	Preferred indications include
			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
_				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP,	Disease"). Preferred
				bind to CREB transcription	indications include
				factor, and modulate	autoimmune diseases (e.g.,
				expression of genes involved	rheumatoid arthritis, systemic

	in a wide variety of cell	lupus erythematosis, multiple
	functions. Exemplary assays	sclerosis and/or as described
	for transcription through the	below), immunodeficiencies
	cAMP response element that	(e.g., as described below),
	may be used or routinely	boosting a T cell-mediated
	 modified to test cAMP-	immune response, and
_	 response element activity of	suppressing a T cell-mediated
-	polypeptides of the invention	immune response. Additional
-	(including antibodies and	preferred indications include
	agonists or antagonists of the	inflammation and
	invention) include assays	inflammatory disorders.
	disclosed in Berger et al., Gene	Highly preferred indications
	66:1-10 (1998); Cullen and	include neoplastic diseases
	Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
	216:362-368 (1992); Henthorn	and/or as described below
	 et al., Proc Natl Acad Sci USA	under "Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
-	 al., Virus Genes 15(2):105-117	indications include neoplasms
-	(1997); and Belkowski et al., J	and cancers, such as, leukemia,
	Immunol 161(2):659-665	lymphoma (e.g., T cell
	(1998), the contents of each of	lymphoma, Burkitt's
	which are herein incorporated	lymphoma, non-Hodgkins
	 by reference in its entirety. T	lymphoma, Hodgkin"s
	cells that may be used	disease), melanoma, and
	according to these assays are	prostate, breast, lung, colon,
	publicly available (e.g.,	pancreatic, esophageal,
	 through the ATCC).	stomach, brain, liver and
	Exemplary human T cells that	urinary cancer. Other preferred
-	may be used according to these	indications include benign
	 assays include the JURKAT	dysproliferative disorders and
	cell line, which is a suspension	pre-neoplastic conditions, such

				culture of leukemia cells that produce IL-2 when stimulated.	as, for example, hyperplasia, metaplasia, and/or dysplasia.
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
			-,-		acute lymphocytic anemia
_					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HNHOD46	749	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
_			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),

-		modulate expression of genes	immunodeficiencies (e.g., as
		involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
	-	NFAT response element that	response. Additional highly
		may be used or routinely	preferred indications include
		modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
	-	agonists or antagonists of the	infectious disease as described
		invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
		66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
	•	et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988); Serfling	"Hyperproliferative
		et al., Biochim Biophys Acta	Disorders"). Preferred
		1498(1):1-18 (2000); De Boer	indications include neoplasms
	1.7	et al., Int J Biochem Cell Biol	and cancers, such as, for
		(31(10):1221-1236 (1999);	example, leukemia, lymphoma,
		Fraser et al., Eur J Immunol	and prostate, breast, lung,
		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		Yeseen et al., J Biol Chem	stomach, brain, liver and
		268(19):14285-14293 (1993),	urinary cancer. Other preferred
		the contents of each of which	indications include benign
		are herein incorporated by	dysproliferative disorders and
	-	reference in its entirety. T	pre-neoplastic conditions, such
		cells that may be used	as, for example, hyperplasia,

			according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HNHOD46	749	Activation of transcription through NFKB response element in immune cells (such as basophils).	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g.,

	agonists or antagonists of the	as described below under
	invention) to regulate NFKB	"Immune Activity", and
	transcription factors and	"Blood-Related Disorders").
	modulate expression of	Preferred indications also
	immunomodulatory genes.	include autoimmune diseases
	Exemplary assays for	(e.g., rheumatoid arthritis,
	transcription through the	systemic lupus erythematosis,
	NFKB response element that	multiple sclerosis and/or as
	may be used or rountinely	described below) and
	modified to test NFKB-	immunodeficiencies (e.g., as
	response element activity of	described below). Preferred
	polypeptides of the invention	indications also include
	(including antibodies and	neoplastic diseases (e.g.,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Berger et al., Gene	below under
	66:1-10 (1998); Cullen and	"Hyperproliferative
	Malm, Methods in Enzymol	Disorders"). Preferred
	216:362-368 (1992); Henthorn	indications include neoplasms
	et al., Proc Natl Acad Sci USA	and cancer, such as, for
-	85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
	et al, Int Arch Allergy	melanoma, and prostate,
	Immunol 114(3):207-17	breast, lung, colon, pancreatic,
	(1997), the contents of each of	esophageal, stomach, brain,
	which are herein incorporated	liver, urinary tract cancers and
	by reference in its entirety.	as described below under
	Basophils that may be used	"Hyperproliferative
	according to these assays are	Disorders".
	publicly available (e.g.,	
	through the ATCC).	
	Exemplary human basophil	

	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, non-Hodgkins sud prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia,
cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the	invention (including antibodies
	Activation of transcription through GAS response element in immune cells (such as T-cells).	
	5 749	
	HNHOD46	

and agonists or antagonists of the invention) include assays
•

				idiopathic pulmonary fibrosis.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				acute lymphocytic anemia
		•		(ALL), plasmacytomas,
				multiple myeloma, arthritis,
	179			AIDS, granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, and
				asthma and allergy.
HNHOD46	749	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include inflammation and
		through NFKB	NFKB response element are	inflammatory disorders.
		response element in	well-known in the art and may	Highly preferred indications
		immune cells (such	be used or routinely modified	include blood disorders (e.g.,
		as T-cells).	to assess the ability of	as described below under
		•	polypeptides of the invention	"Immune Activity", "Blood-
			(including antibodies and	Related Disorders", and/or
			agonists or antagonists of the	"Cardiovascular Disorders").
			invention) to regulate NFKB	Highly preferred indications
			transcription factors and	include autoimmune diseases
			modulate expression of	(e.g., rheumatoid arthritis,
			immunomodulatory genes.	systemic lupus erythematosis,

multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred	indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases	(e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for	example, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also
Exemplary assays for may be used or rountinely may be used to test NFKB- according to the modified to test NFKB- according to test NFKB- according to the modified to test NFKB- according to test NFKB- according to test NFKB- according to the modified to the modi	f on iene	1	29(3):838-844 (1999), the contents of each of which are calculated by herein incorporated by reference in its entirety. Exemplary human T cells, escuch as the MOLT4, that may live used according to these passays are publicly available be calculated. (e.g., through the ATCC).
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include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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	HNHOD46

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"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases	(e.g., rheumatoid artifilis, systemic lupus erythematosis, Crohn's disease, multiple	below), immunodeficiencies (e.g., as described below),	boosting a 1 cell-mediated immune response, and suppressing a T cell-mediated	immune response. Additional	include inflammation and	inflammatory disorders, and treating ioint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis. Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,
genes in many cell types. Exemplary assays for transcription through the SRE	that may be used or routinely modified to test SRE activity of the polypeptides of the	invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm Methods in Enzymol	216:362-368 (1992); Henthorn	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cvtotoxic activity.
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	I	malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
_		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
	1	neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues, hemophilia,
		hypercoagulation, diabetes
	1	mellitus, endocarditis,
		meningitis, Lyme Disease,
		cardiac reperfusion injury, and
		asthma and allergy. An
		additional preferred indication

					is infection (e.g., an infectious disease as described below under "Infectious Disease").
	HNHOD46	749	Activation of transcription	Assays for the activation of transcription through the	Highly preferred indications include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
_				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
	_			polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
_				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
				216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative

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Disorders"). Highly preferred indications include neoplasms and cancers, such as, for	carcinoma, leukemia, renal central carcinoma, leukemia, lymphoma, and prostate,	esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative	disorders and pre-neopiasue conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia.	Preferred indications also include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL),		myeloma, Burklıt s tympholita, arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	heutrophilia, psoriasis, hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune	reactions to transplanted
85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997);	Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844	(1999), the contents of each of which are herein incorporated by reference in its entirety.	NK cells that may be used according to these assays are	publicly available (e.g., through the ATCC).	Exemplary human NK cells that may be used according to	these assays include the NKL	natural killer cell line	established from the peripheral blood of a patient with large	granular lymphocytic	leukemia. This IL-2 dependent suspension culture cell line has	a morphology resembling that	of activated NK cells.					
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					organs, asthma and allergy.
	HNHOD46	749	Activation of	Assays for the activation of	Preferred indications
			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are well-	(e.g., as described below under
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
				polypeptides of the invention	"Immune Activity",
				(including antibodies and	"Cardiovascular Disorders",
				agonists or antagonists of the	and/or "Blood-Related
				invention) to modulate growth	Disorders"), and infection
_				and other cell functions.	(e.g., an infectious disease as
				Exemplary assays for	described below under
				transcription through the AP1	"Infectious Disease"). Highly
				response element that may be	preferred indications include
				used or routinely modified to	autoimmune diseases (e.g.,
				test AP1-response element	rheumatoid arthritis, systemic
				activity of polypeptides of the	lupus erythematosis, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below) and
				the invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications
				Malm, Methods in Enzymol	include inflammation and
				216:362-368 (1992); Henthorn	inflammatory disorders.
				et al., Proc Natl Acad Sci USA	Highly preferred indications
				85:6342-6346 (1988);	also include neoplastic
				Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
				272(49):30806-30811 (1997);	lymphoma, and/or as described
				Chang et al., Mol Cell Biol	below under
		:		18(9):4986-4993 (1998); and	"Hyperproliferative

				Fraser et al., Eur J Immunol	Disorders"). Highly preferred
				29(3):838-844 (1999), the	indications include neoplasms
				contents of each of which are	and cancers, such as, leukemia,
				herein incorporated by	lymphoma, prostate, breast,
				reference in its entirety.	lung, colon, pancreatic,
				Human T cells that may be	esophageal, stomach, brain,
				used according to these assays	liver, and urinary cancer. Other
				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
	•			line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
				responsive suspension-culture	Preferred indications include
				cell line.	arthritis, asthma, AIDS,
	-				allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
_					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression of
					immune reactions to
					transplanted organs and
					tissues, endocarditis,
:					meningitis, and Lyme Disease.
	HNHOD46	749	Activation of	Assays for the activation of	A highly preferred
			transcription	transcription through the CD28	embodiment of the invention
			through CD28	response element are well-	includes a method for

	response element in	known in the art and may be	stimulating T cell proliferation.
	immune cells (such	used or routinely modified to	An alternative highly preferred
	as T-cells).	assess the ability of	embodiment of the invention
		polypeptides of the invention	includes a method for
		(including antibodies and	inhibiting T cell proliferation.
		agonists or antagonists of the	A highly preferred
		invention) to stimulate IL-2	embodiment of the invention
		expression in T cells.	includes a method for
		Exemplary assays for	activating T cells. An
		transcription through the CD28	alternative highly preferred
		response element that may be	embodiment of the invention
-		used or routinely modified to	includes a method for
		test CD28-response element	inhibiting the activation of
		activity of polypeptides of the	and/or inactivating T cells.
		invention (including antibodies	A highly preferred
		and agonists or antagonists of	embodiment of the invention
		the invention) include assays	includes a method for
		disclosed in Berger et al., Gene	stimulating (e.g., increasing)
		66:1-10 (1998); Cullen and	IL-2 production. An alternative
		Malm, Methods in Enzymol	highly preferred embodiment
		216:362-368 (1992); Henthorn	of the invention includes a
		et al., Proc Natl Acad Sci USA	method for inhibiting (e.g.,
		85:6342-6346 (1988);	reducing) IL-2 production.
		McGuire and Iacobelli, J	Additional highly preferred
		Immunol 159(3):1319-1327	indications include
		(1997); Parra et al., J Immunol	inflammation and
		166(4):2437-2443 (2001); and	inflammatory disorders.
		Butscher et al., J Biol Chem	Highly preferred indications
		3(1):552-560 (1998), the	include autoimmune diseases
		contents of each of which are	(e.g., rheumatoid arthritis,
		herein incorporated by	systemic lupus erythematosis,

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multiple sclerosis and/or as	described below), immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	below under	w.Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal	cell carcinoma (e.g., metastatic	renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma), and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example hyperplasia
reference in its entirety. T	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.		4-7																		
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metaplasia, and/or dysplasia.	A fightly preferred indication includes infection (e.g.,	AIDS, tuberculosis, infections	associated with granulomatous	disease, and osteoporosis,	and/or as described below	under "Infectious Disease"). A	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,	psoriasis, and tropical spastic	paraparesis. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, granulomatous
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disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, nelanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative conditions, such as, for	example, nyperplasia, metaplasia, and/or dysplasia. Preferred indications include
disease, neutrop hyperco mellitus mening asthma	Highly include (e.g., le and/or a under " under " Disorde indicati and can exampla (e.g., T Burkitt' Hodgki melano breast, lesophag liver an preferre benign disorde conditic	example metapla Preferre autoimi
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	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the	invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene
		and ag
	of nn AS ement in Ils (such	
	Activation of transcription through GAS response element in immune cells (such as T-cells).	
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	HNHOD46	

rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies	(e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated	immune response. Additional preferred indications include inflammation and inflammatory disorders.	Highly preferred indications include blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with	chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious	Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia,
66:1-10 (1998); Cullen and rhalm, Methods in Enzymol lul 216:362-368 (1992); Henthorn sciet al Proc Natl Acad Sci USA be		the re	nat Se	assays are publicly available "It (e.g., through the ATCC). Re "C "C "C "C "C "It information in the analysis of the state	ch dis os int int	Di pre idi idi Pre
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			may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HNHOD46	749	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as

	may be used or rountinely	described below). An
	modified to test NFKB-	additional highly preferred
	response element activity of	indication is infection (e.g.,
	polypeptides of the invention	AIDS, and/or an infectious
	(including antibodies and	disease as described below
	agonists or antagonists of the	under "Infectious Disease").
	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
 	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Gnes 15(2):105-117	indications include neoplasms
 	(1997); and Fraser et al.,	and cancers, such
	29(3):838-844 (1999), the	as,melanoma, renal cell
	contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
	reference in its entirety. T	breast, lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is a suspension	metaplasia, and/or dysplasia.
	culture of IL-2 and IL-4	Preferred indications also
	responsive T cells.	include anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute

element that may be used or	lupus erythematosis, multiple
routinely modified to test	sclerosis and/or as described
STAT6 response element	below) and
activity of the polypeptides of	immunodeficiencies (e.g., as
the invention (including	described below).
antibodies and agonists or	Preferred indications include
antagonists of the invention)	neoplastic diseases (e.g.,
include assays disclosed in	leukemia, lymphoma,
Berger et al., Gene 66:1-10	melanoma, and/or as described
(1998); Cullen and Malm,	below under
Methods in Enzymol 216:362-	"Hyperproliferative
368 (1992); Henthorn et al.,	Disorders"). Preferred
Proc Natl Acad Sci USA	indications include neoplasms
 85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
(1998); Moffatt et al.,	prostate, breast, lung, colon,
Transplantation 69(7):1521-	pancreatic, esophageal,
1523 (2000); Curiel et al., Eur	stomach, brain, liver and
J Immunol 27(8):1982-1987	urinary cancer. Other preferred
(1997); and Masuda et al., J	indications include benign
Biol Chem 275(38):29331-	dysproliferative disorders and
29337 (2000), the contents of	pre-neoplastic conditions, such
each of which are herein	as, for example, hyperplasia,
incorporated by reference in its	metaplasia, and/or dysplasia.
entirety. T cells that may be	Preferred indications include
used according to these assays	anemia, pancytopenia,
 are publicly available (e.g.,	leukopenia, thrombocytopenia,
 through the ATCC).	Hodgkin's disease, acute
Exemplary T cells that may be	lymphocytic anemia (ALL),
 used according to these assays	plasmacytomas, multiple
include the SUPT cell line,	myeloma, Burkitt's lymphoma,

			which is a suspension culture of IL-2 and IL-4 responsive T cells.	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
HNHOG73	750	Activation of transcription through cAMP response element (CRE) in preadipocytes.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease
			in a wide variety of cell functions. For example, a	(e.g., renal failure, nephropathy and/or other

3T3-L1/CRE renorter assav	diseases and disorders as
may be used to identify factors	described in the "Renal
that activate the cAMP	Disorders" section below),
signaling pathway. CREB	diabetic neuropathy, nerve
plays a major role in	disease and nerve damage
adipogenesis, and is involved	(e.g., due to diabetic
in differentiation into	neuropathy), blood vessel
adipocytes. CRE contains the	blockage, heart disease, stroke,
binding sequence for the	impotence (e.g., due to diabetic
 transcription factor CREB	neuropathy or blood vessel
(CRE binding protein).	blockage), seizures, mental
Exemplary assays for	confusion, drowsiness,
transcription through the	nonketotic hyperglycemic-
 cAMP response element that	hyperosmolar coma,
may be used or routinely	cardiovascular disease (e.g.,
modified to test cAMP-	heart disease, atherosclerosis,
 response element activity of	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
 (including antibodies and	diseases and disorders as
 agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	section below), dyslipidemia,
66:1-10 (1998); Cullen and	endocrine disorders (as
Malm, Methods in Enzymol	described in the "Endocrine
216:362-368 (1992); Henthorn	Disorders" section below),
et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
et al., Mol Cell Biol	blindness), ulcers and impaired
20(3):1008-1020 (2000); and	wound healing, and infection
Klemm et al., J Biol Chem	(e.g., infectious diseases and
273:917-923 (1998), the	disorders as described in the

			contents of each of which are	"Infectious Diseases" section
			herein incorporated by	below, especially of the
			reference in its entirety. Pre-	urinary tract and skin), carpal
			adipocytes that may be used	tunnel syndrome and
			according to these assays are	Dupuytren's contracture).
			publicly available (e.g.,	Additional highly preferred
			through the ATCC) and/or	indications are complications
			may be routinely generated.	associated with insulin
			Exemplary mouse adipocyte	resistance.
			cells that may be used	
			according to these assays	
			include 3T3-L1 cells. 3T3-L1	
			is an adherent mouse	
			preadipocyte cell line that is a	
			continuous substrain of 3T3	
			fibroblast cells developed	
			through clonal isolation and	
			undergo a pre-adipocyte to	
			adipose-like conversion under	
			appropriate differentiation	
			conditions known in the art.	
HNHOG73	750	Activation of	This reporter assay measures	Highly preferred indication
		transcription	activation of the NFkB	includes allergy, asthma, and
		through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
		response element in	human basophil cell line.	preferred indications include
		immune cells (such	Assays for the activation of	infection (e.g., an infectious
		as basophils).	transcription through the	disease as described below
			NFKB response element are	under "Infectious Disease"),
			well-known in the art and may	and inflammation and
			be used or routinely modified	inflammatory disorders.
			to assess the ability of	Preferred indications include

		polypeptides of the invention	immunological and
		(including antibodies and	hempatopoietic disorders (e.g.,
		agonists or antagonists of the	as described below under
		invention) to regulate NFKB	"Immune Activity", and
		transcription factors and	"Blood-Related Disorders").
		modulate expression of	Preferred indications also
		immunomodulatory genes.	include autoimmune diseases
	-	Exemplary assays for	(e.g., rheumatoid arthritis,
		transcription through the	systemic lupus erythematosis,
		NFKB response element that	multiple sclerosis and/or as
		may be used or rountinely	described below) and
		modified to test NFKB-	immunodeficiencies (e.g., as
		response element activity of	described below). Preferred
		polypeptides of the invention	indications also include
		(including antibodies and	neoplastic diseases (e.g.,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Berger et al., Gene	below under
		66:1-10 (1998); Cullen and	"Hyperproliferative
		Malm, Methods in Enzymol	Disorders"). Preferred
		216:362-368 (1992); Henthorn	indications include neoplasms
		et al., Proc Natl Acad Sci USA	and cancer, such as, for
		85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
		et al, Int Arch Allergy	melanoma, and prostate,
		Immunol 114(3):207-17	breast, lung, colon, pancreatic,
-		(1997), the contents of each of	esophageal, stomach, brain,
		which are herein incorporated	liver, urinary tract cancers and
		by reference in its entirety.	as described below under
		Basophils that may be used	"Hyperproliferative
		according to these assays are	Disorders".
		publicly available (e.g.,	

				through the ATCC). Exemplary human basophil	
				cell lines that may be used	
				according to these assays	
				include Ku812, originally	
				established from a patient with	
	-			chronic myelogenous	
				leukemia. It is an immature	
				prebasophilic cell line that can	
				be induced to differentiate into	
				mature basophils.	
	HNHOG73	750	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
	_		cells).	the ability of polypeptides of	of the invention includes a
-				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
			-	genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,

		of the polyneptides of the	Crohn"s disease, multiple
		invention (including antibodies	sclerosis and/or as described
		and agonists or antagonists of	below), immunodeficiencies
		the invention) include assays	(e.g., as described below),
		disclosed in Berger et al., Gene	boosting a T cell-mediated
		66:1-10 (1998); Cullen and	immune response, and
		Malm, Methods in Enzymol	suppressing a T cell-mediated
	_	216:362-368 (1992); Henthorn	immune response. Additional
		et al., Proc Natl Acad Sci USA	highly preferred indications
		85:6342-6346 (1988); Benson	include inflammation and
		et al., J Immunol 153(9):3862-	inflammatory disorders, and
		3873 (1994); and Black et al.,	treating joint damage in
		Virus Genes 12(2):105-117	patients with rheumatoid
		(1997), the content of each of	arthritis. An additional highly
-		which are herein incorporated	preferred indication is sepsis.
		by reference in its entirety. T	Highly preferred indications
		cells that may be used	include neoplastic diseases
		according to these assays are	(e.g., leukemia, lymphoma,
		publicly available (e.g.,	and/or as described below
		through the ATCC).	under "Hyperproliferative
		Exemplary T cells that may be	Disorders"). Additionally,
		used according to these assays	highly preferred indications
		include the NK-YT cell line,	include neoplasms and
		which is a human natural killer	cancers, such as, for example,
		cell line with cytolytic and	leukemia, lymphoma,
		cytotoxic activity.	melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other

			cell 2B9		
	HNTBI26	751	Production of IL-8	Assays measuring production	Highly preferred indications
			by by endothelial	of 1L-8 are well known in the	include immunological and
			cells (such as	art and may be used or	inflammatory disorders (e.g.,
			Human Umbilical	routinely modified to assess	such as allergy, asthma,
			Cord Endothelial	the ability of polypeptides of	leukemia, etc. and as described
			Cells).	the invention (including	below under "Immune
				antibodies and agonists or	Activity", and "Blood-Related
				antagonists of the invention) to	Disorders"). Highly preferred
				regulate production and/or	indications also includie
				secretion of IL-8. For	autoimmune disorders (e.g.,
				example, FMAT may be used	rheumatoid arthritis, systemic
				or routinely modified to assess	lupus erythematosis, Crohn"s
				the ability of polypeptides of	disease, multiple sclerosis
				the invention (including	and/or as described below),
				antibodies and agonists or	neoplastic disorders (e.g.,
				antagonists of the invention) to	organ cancers such as lung,
				regulate production and/or	liver, colon cancer, and/or as
			-	secretion of IL-8 from	described below under
				endothelial cells (such as	"Hyperproliferative
				human umbilical vein	Disorders"), and
				endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
				HUVECs are endothelial cells	such as described below under
				which line venous blood	"Cardiovascular Disorders").
				vessels, and are involved in	Preferred indications include
				functions that include, but are	thrombosis, bacteremia and
				not limited to, angiogenesis,	sepsis syndrome and
•				vascular permeability, vascular	consequent complications
				tone, and immune cell	(such as acute respiratory
				extravasation. Endothelial	distress syndrome and
				cells play a pivotal role in the	systemic ischemia-reperfusion

				initiation and perpetuation of inflammation and secretion of IL-8 may play an important role in recruitment and activation of immune cells such as neutrophils, macrophages, and lymphocytes.	resulting from septic shock), restnosis and atherosclerosis.
H	HNTBI26	751	IL-8 in Normal Human Bronchial Epitheliae		
<u>H</u>	HNTBI26	751	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and progression of diabetes. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of propreentides of the invention	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, importence (e.g., due to diabetic
				(including antibodies and agonists or antagonists of the	neuropathy or blood vessel blockage), seizures, mental

F		eth, AC, et nonketotic hyperglycemic-	0(3):285-8 hyperosmolar coma,						, et al., described in the	1 1:S44-7 "Cardiovascular Disorders"	al., J section below), dyslipidemia,		et al., FEBS described in the "Endocrine			199); Lee et (e.g., diabetic retinopathy and		ည			nb 3(2): 75- "Infectious Diseases" section	itents of each below, especially of the		ference in its tunnel syndrome and	ic cells that Dupuytren's contracture).		y available indication is obesity and/or	ATCC) complications associated with		olary preferred indications include	at may be weight loss or alternatively
/ .	invention) include the assays	disclosed in: Loweth, AC, et	al., FEBS Lett, 400(3):285-8	(1997); Saini, KS, et al.,	Biochem Mol Biol Int,	39(6):1229-36 (1996);	Krautheim, A., et al., Br J	Pharmacol, 129(4):687-94	(2000); Chandra J, et al.,	Diabetes, 50 Suppl 1:S44-7	(2001); Suk K, et al., J	Immunol, 166(7):4481-9	(2001); Tejedo J, et al., FEBS	Lett, 459(2):238-43 (1999);	Zhang, S., et al., FEBS Lett,	455(3):315-20 (1999); Lee et	al., FEBS Lett 485(2-3): 122-	126 (2000); Nor et al., J Vasc	Res 37(3): 209-218 (2000);	and Karsan and Harlan, J	Atheroscler Thromb 3(2): 75-	80 (1996); the contents of each	of which are herein	incorporated by reference in its	entirety. Pancreatic cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC)	and/or may be routinely	generated. Exemplary	hancreatic cells that may be
		-													-							-									

				used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta cell insulinoma cell line derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al.	weight gain. highly preferred indications are complications associated with insulin resistance.
H H	HNTBI26	751	Caspase (+paclitaxel) in SW480	.7.5517.	
H	HNTBL27	752	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is associated with induction and	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),

	Exemplary assays for caspase	or caspase	disease and nerve damage
	apoptosis that may be used or	be used or	(e.g., due to diabetic
	routinely modified to test	o test	neuropathy), blood vessel
	capase apoptosis activity of	ivity of	blockage, heart disease, stroke,
	polypeptides of the invention	invention	impotence (e.g., due to diabetic
	(including antibodies and	s and	neuropathy or blood vessel
	agonists or antagonists of the	sts of the	blockage), seizures, mental
	invention) include the assays	he assays	confusion, drowsiness,
	disclosed in: Loweth, AC, et	h, AC, et	nonketotic hyperglycemic-
	al., FEBS Lett, 400(3):285-8	(3):285-8	hyperosmolar coma,
	(1997); Saini, KS, et al.,	t al.,	cardiovascular disease (e.g.,
	Biochem Mol Biol Int,	nt,	heart disease, atherosclerosis,
	39(6):1229-36 (1996);	6);	microvascular disease,
	Krautheim, A., et al., Br J	"BrJ	hypertension, stroke, and other
	Pharmacol, 129(4):687-94	587-94	diseases and disorders as
	(2000); Chandra J, et al.,	st al.,	described in the
	Diabetes, 50 Suppl 1:S44-7	1:S44-7	"Cardiovascular Disorders"
	(2001); Suk K, et al., J	., J	section below), dyslipidemia,
-	Immunol, 166(7):4481-9	81-9	endocrine disorders (as
	(2001); Tejedo J, et al., FEBS	al., FEBS	described in the "Endocrine
	Lett, 459(2):238-43 (1999);	(1999);	Disorders" section below),
	Zhang, S., et al., FEBS Lett,	BS Lett,	neuropathy, vision impairment
	(455(3):315-20 (1999); Lee et	9); Lee et	(e.g., diabetic retinopathy and
	al., FEBS Lett 485(2-3): 122-	2-3): 122-	blindness), ulcers and impaired
	126 (2000); Nor et al., J Vasc	ıl., J Vasc	wound healing, and infection
	Res 37(3): 209-218 (2000);	(2000);	(e.g., infectious diseases and
	and Karsan and Harlan, J	lan, J	disorders as described in the
	Atheroscler Thromb 3(2): 75-	3(2): 75-	"Infectious Diseases" section
	80 (1996); the contents of each	nts of each	below, especially of the
	of which are herein		urinary tract and skin), carpal
	incorporated by reference in its	rence in its	tunnel syndrome and

			entirety. Pancreatic cells that may be used according to these assays are publicly available	Dupuytren's contracture). An additional highly preferred indication is obesity and/or
			(e.g., through the ATCC) and/or may be routinely	complications associated with obesity. Additional highly
			generated. Exemplary	preferred indications include
			pancreatic cells that may be	weight loss or alternatively,
			include RIN-m. RIN-m is a	highly preferred indications are
			rat adherent pancreatic beta	complications associated with
			cell insulinoma cell line	insulin resistance.
			derived from a radiation	
			induced transplantable rat islet	
			cell tumor. The cells produce	
			and secrete islet polypeptide	
			hormones, and produce insulin,	
			somatostatin, and possibly	
			glucagon. ATTC: #CRL-2057	
			Chick et al. Proc. Natl. Acad.	
			Sci. 1977 74:628; AF et al.	
			Proc. Natl. Acad. Sci. 1980	
			77:3519.	
HNTBL27	752	Production of IL-10	Assays for production of IL-10	Highly preferred indications
		and activation of T-	and activation of T-cells are	include allergy and asthma.
		cells.	well known in the art and may	Additional highly preferred
			be used or routinely modified	indications include immune
			to assess the ability of	and hematopoietic disorders
			polypeptides of the invention	(e.g., as described below under
			(including antibodies and	"Immune Activity", and
			agonists or antagonists of the	"Blood-Related Disorders"),
			invention) to stimulate or	autoimmune diseases (e.g.,

of II10 rheumatoid arthritis, systemic	•	pe		of immunodeficiencies (e.g., as		luding cell-mediated immune	onists of the response, and suppressing a T		T-cell response.	ide, for	uch as	ited in:	al., "Th-2	gic disease"	(4): 956-968	, et al., "T-	-directed	a"	Therapeutics;	0); the	of which are	ed by	entirety.	hat may be	these assays	IL10	cells may be	rker of Th2	Th2 cells are	
inhihit production of II - 10	and/or activation of T-cells.	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	

	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis.
IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary
	Production of TNF alpha by dendritic cells
	753
	HNTCE26

				- -															73			_	-
systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described	(e.g., as described below), hoosting a T cell-mediated	immune response, and	immune response. Additional	highly preferred indications include inflammation and	inflammatory disorders, and	treating joint damage in patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	1:100 and minimum Othon
immunomodulatory proteins evaluate the production of cytokines such as tumor	and the induction or inhibition of an inflammatory or	cytotoxic response. Such	routinely modified to test	immunomodulatory activity of polypeptides of the invention	(including antibodies and	agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Verhasselt et al., Eur J	Immunol 28(11):3886-3890	(1198); Dahlen et al., J	Immunol 160(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Unmon dandritic calle that may
									_														

			be used according to these assays may be isolated using	preferred indications include benign dysproliferative
			techniques disclosed herein or	disorders and pre-neoplastic
			otherwise known in the art.	conditions, such as, for
		~	Human dendritic cells are	example, hyperplasia,
		-	antigen presenting cells in	metaplasia, and/or dysplasia.
			suspension culture, which,	Preferred indications include
			when activated by antigen	anemia, pancytopenia,
			and/or cytokines, initiate and	leukopenia, thrombocytopenia,
			upregulate T cell proliferation	Hodgkin's disease, acute
			and functional activities.	lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
		-		arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
		-		suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HNTCE26	753	CD69 in Human T cells		

HNTCE26	753	Stimulation of	Assays for measuring secretion	A highly preferred
	-	insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
	-	from pancreatic	the art and may be used or	An additional highly preferred
		beta cells.	routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
			is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
			disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
	.		used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-
			secretion (from pancreatic	hyperosmolar coma,
			cells) by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,
	_		and agonists or antagonists of	microvascular disease,
		-	the invention) include assays	hypertension, stroke, and other
			disclosed in: Ahren, B., et al.,	diseases and disorders as
			Am J Physiol, 277(4 Pt	described in the
			2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
			al., Endocrinology,	section below), dyslipidemia,

		be used or routinely modified to assess the ability of	(or antibodies, agonists, or antagonists thereof) in
		polypeptides of the invention	detection, diagnosis,
		(including antibodies and	prevention, and/or treatment of
		agonists or antagonists of the	Inflammation, Vascular
		invention) to regulate ICAM-1	Disease, Athereosclerosis,
		expression. Exemplary assays	Restenosis, and Stroke
		that may be used or routinely	
		modified to measure ICAM-1	
		expression include assays	
	-	disclosed in: Takacs P, et al,	
		FASEB J, 15(2):279-281	
		(2001); and, Miyamoto K, et	
		al., Am J Pathol, 156(5):1733-	
		1739 (2000), the contents of	
		each of which is herein	
		incorporated by reference in its	
		entirety. Cells that may be	
		used according to these assays	
		are publicly available (e.g.,	
		through the ATCC) and/or	
		may be routinely generated.	
_		Exemplary cells that may be	
		used according to these assays	
		include microvascular	
		endothelial cells (MVEC).	
754	Regulation of	Assays for the regulation of	A highly preferred indication
	transcription via	transcription through the	is diabetes mellitus.
	DMEF1 response	DMEF1 response element are	Additional highly preferred
	element in	well-known in the art and may	indications include
	adipocytes and pre-	be used or routinely modified	complications associated with

		adipocytes	to assess the ability of	diabetes (e.g., diabetic
		•	polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
	_		invention) to activate the	nephropathy and/or other
			DMEF1 response element in a	diseases and disorders as
			reporter construct (such as that	described in the "Renal
			containing the GLUT4	Disorders" section below),
			promoter) and to regulate	diabetic neuropathy, nerve
			insulin production. The	disease and nerve damage
		***	DMEF1 response element is	(e.g., due to diabetic
			present in the GLUT4	neuropathy), blood vessel
			promoter and binds to MEF2	blockage, heart disease, stroke,
			transcription factor and another	impotence (e.g., due to diabetic
			transcription factor that is	neuropathy or blood vessel
			required for insulin regulation	blockage), seizures, mental
			of Glut4 expression in skeletal	confusion, drowsiness,
-			muscle. GLUT4 is the primary	nonketotic hyperglycemic-
			insulin-responsive glucose	hyperosmolar coma,
			transporter in fat and muscle	cardiovascular disease (e.g.,
	•••		tissue. Exemplary assays that	heart disease, atherosclerosis,
			may be used or routinely	microvascular disease,
			modified to test for DMEF1	hypertension, stroke, and other
			response element activity (in	diseases and disorders as
			adipocytes and pre-adipocytes)	described in the
			by polypeptides of the	"Cardiovascular Disorders"
			invention (including antibodies	section below), dyslipidemia,
			and agonists or antagonists of	endocrine disorders (as
			the invention) include assays	described in the "Endocrine
			disclosed inThai, M.V., et al., J	Disorders" section below),
			Biol Chem, 273(23):14285-92	neuropathy, vision impairment

		(1998): Mora. S., et al., J Biol	al. J Biol	(e.g., diabetic retinopathy and
		Chem, 275(21):16323-8	3-8	blindness), ulcers and impaired
		(2000); Liu, M.L., et al., J Biol	al., J Biol	wound healing, and infection
		Chem, 269(45):28514-21	4-21	(e.g., infectious diseases and
		(1994); "Identification of a 30-	on of a 30-	disorders as described in the
		base pair regulatory element	element	"Infectious Diseases" section
		and novel DNA binding	ling	below, especially of the
		protein that regulates the	s the	urinary tract and skin). An
		human GLUT4 promoter in	noter in	additional highly preferred
		transgenic mice", J Biol Chem.	3iol Chem.	indication is obesity and/or
		2000 Aug 4;275(31):23666-73;	:23666-73;	complications associated with
		Berger, et al., Gene 66:1-10	66:1-10	obesity. Additional highly
	**	(1988); and, Cullen, B., et al.,	B., et al.,	preferred indications include
		Methods in Enzymol.	I	weight loss or alternatively,
		216:362–368 (1992), the	, the	weight gain. Additional highly
		contents of each of which is	which is	preferred indications are
		herein incorporated by	by	complications associated with
		reference in its entirety.	ety.	insulin resistance.
		Adipocytes and pre-adipocytes	adipocytes	
		that may be used according to	cording to	
-		these assays are publicly	licly	
		available (e.g., through the	igh the	
		ATCC) and/or may be	be	
		routinely generated.		
		Exemplary cells that may be	t may be	
		used according to these assays	ese assays	
		include the mouse 3T3-L1 cell	T3-L1 cell	
		line which is an adherent	erent	
		mouse preadipocyte cell line.	cell line.	
		Mouse 3T3-L1 cells are a	are a	
		continuous substrain of 3T3	1 of 3T3	

	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel
fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved	in differentiation into adipocytes. CRE contains the binding sequence for the transcription factor CREB
	Activation of transcription through cAMP response element (CRE) in preadipocytes.	
	754	
	HNTNI01	

	(CRE hinding protein)	blockage) seizures mental
	vomplem, occove for	conflicion drowsiness
	Exciliplally assays for	Collination, diowaliteas,
	transcription through the	nonketotic hyperglycemic-
73	cAMP response element that	hyperosmolar coma,
<u>u</u>	may be used or routinely	cardiovascular disease (e.g.,
<u>u</u>	modified to test cAMP-	heart disease, atherosclerosis,
a.	response element activity of	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
(i)	(including antibodies and	diseases and disorders as
38	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
lp	disclosed in Berger et al., Gene	section below), dyslipidemia,
99	66:1-10 (1998); Cullen and	endocrine disorders (as
2	Malm, Methods in Enzymol	described in the "Endocrine
	216:362-368 (1992); Henthorn	Disorders" section below),
	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
- et	et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3):1008-1020 (2000); and	wound healing, and infection
<u>X</u>	Klemm et al., J Biol Chem	(e.g., infectious diseases and
2.	273:917-923 (1998), the	disorders as described in the
5	contents of each of which are	"Infectious Diseases" section
<u>q</u>	herein incorporated by	below, especially of the
1.6	reference in its entirety. Pre-	urinary tract and skin), carpal
æ	adipocytes that may be used	tunnel syndrome and
	according to these assays are	Dupuytren's contracture).
<u>C.</u>	publicly available (e.g.,	Additional highly preferred
 	through the ATCC) and/or	indications are complications
ш	may be routinely generated.	associated with insulin
ш_	Exemplary mouse adipocyte	resistance.
3	cells that may be used	

according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	transcription through the serum Response Element in (SRE) are well-known in the ability of polypeptides of antibodies and agonists or regulate the serum response antibodies and modulate the expression of genes involved in growth. Exemplary assays for transcription through the invention (including activity of the polypeptides of the invention through the ability of polypeptides of antibodies and agonists or alternatively, weight gain. An additional highly preferred indication is a complication regulate the serum response factors and modulate the ability of genes involved in growth. Exemplary assays for transcription through the section below), the invention (including diabetic neuropathy, nerve
	transcription through serum response element in pre-adipocytes.
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		antagonists of the invention)	(e.g., due to diabetic
		include assays disclosed in	neuropathy), blood vessel
		Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
		(1998); Cullen and Malm,	impotence (e.g., due to diabetic
		Methods in Enzymol 216:362-	neuropathy or blood vessel
		368 (1992); Henthorn et al.,	blockage), seizures, mental
		Proc Natl Acad Sci USA	confusion, drowsiness,
		85:6342-6346 (1988); and	nonketotic hyperglycemic-
		Black et al., Virus Genes	hyperosmolar coma,
		12(2):105-117 (1997), the	cardiovascular disease (e.g.,
		content of each of which are	heart disease, atherosclerosis,
		herein incorporated by	microvascular disease,
		reference in its entirety. Pre-	hypertension, stroke, and other
		adipocytes that may be used	diseases and disorders as
		according to these assays are	described in the
		publicly available (e.g.,	"Cardiovascular Disorders"
		through the ATCC) and/or	section below), dyslipidemia,
		may be routinely generated.	endocrine disorders (as
		Exemplary mouse adipocyte	described in the "Endocrine
		cells that may be used	Disorders" section below),
		according to these assays	neuropathy, vision impairment
		include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
		is an adherent mouse	blindness), ulcers and impaired
		preadipocyte cell line that is a	wound healing, and infection
		continuous substrain of 3T3	(e.g., infectious diseases and
		fibroblast cells developed	disorders as described in the
		through clonal isolation and	"Infectious Diseases" section
		undergo a pre-adipocyte to	below). Additional highly
	-	adipose-like conversion under	preferred indications are
		appropriate differentiation	complications associated with
_		conditions known in the art.	insulin resistance.

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93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed	and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol
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			-											-				-				-				_				

	Highly preferred indications include asthma, allergy, hypersensitivity reactions, and inflammation. Preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), immunological disorders, inflammation and
Chem; Oct 20;275(42):33167-75 (2000); the contents of each of which are herein incorporated by reference in its entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB
·	Activation of transcription through NFKB response element in immune cells (such as EOL1 cells).
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			EOL-1 cells) may link the NFKB element to a repeorter gene and binds to the NFKB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human	
HNTNI01	754	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisnis	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve

	stimulted by insulin. ME	disease and nerve damage
	promoter contains two direct	(e.g., due to diabetic
	repeat (DR1)- like elements	neuropathy), blood vessel
	MEp and MEd identified as	blockage, heart disease, stroke,
	putative PPAR response	impotence (e.g., due to diabetic
	elements. ME promoter may	neuropathy or blood vessel
	also responds to AP1 and other	blockage), seizures, mental
	transcription factors.	confusion, drowsiness,
	Exemplary assays that may be	nonketotic hyperglycemic-
	used or routinely modified to	hyperosmolar coma,
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	heart disease, atherosclerosis,
	(in adipoocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
_	8004 (1999); Ijpenberg, A., et	wound healing, and infection
	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and

			contents of each of which is	Dupuytren's contracture).
			herein incorporated by	An additional highly preferred
			reference in its entirety.	indication is obesity and/or
			Hepatocytes that may be used	complications associated with
			according to these assays are	obesity. Additional highly
			publicly available (e.g.,	preferred indications include
			through the ATCC) and/or	weight loss or alternatively,
			may be routinely generated.	weight gain. Aditional
			Exemplary hepatocytes that	highly preferred indications are
			may be used according to these	complications associated with
			assays includes the H4IIE rat	insulin resistance.
			liver hepatoma cell line.	
 HNTNI01	754	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the GATA-3	include allergy, asthma, and
		through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
			through the GATA3 response	Preferred indications also
			element are well-known in the	include blood disorders (e.g.,
			art and may be used or	as described below under
			routinely modified to assess	"Immune Activity", "Blood-
			the ability of polypeptides of	Related Disorders", and/or
			the invention (including	"Cardiovascular Disorders").
			antibodies and agonists or	Preferred indications include
			antagonists of the invention) to	autoimmune diseases (e.g.,
			regulate GATA3 transcription	rheumatoid arthritis, systemic
			factors and modulate	lupus erythematosis, multiple

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sclerosis and/or as described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,
expression of mast cell genes important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are
		_																									· · ·		
					_																								

			publicly available (e.g., through the ATCC).	suppression of immune reactions to transplanted
			Exemplary human mast cells	organs and tissues, hemophilia,
			that may be used according to	hypercoagulation, diabetes
			these assays include the HMC-	mellitus, endocarditis,
			1 cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
	_		cell leukemia, and exhibits	
	•••		many characteristics of	
			immature mast cells.	
 HNTNI01	754	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and
	_		activation of transcription	inflammatory disorders.
		-	through the Nuclear Factor of	Preferred indications also
			Activated T cells (NFAT)	include blood disorders (e.g.,
			response element are well-	as described below under
			known in the art and may be	"Immune Activity", "Blood-
			used or routinely modified to	Related Disorders", and/or
			assess the ability of	"Cardiovascular Disorders").
			polypeptides of the invention	Preferred indications include
			(including antibodies and	autoimmune diseases (e.g.,
			agonists or antagonists of the	rheumatoid arthritis, systemic
			invention) to regulate NFAT	lupus erythematosis, multiple

transcription factors and	sclerosis and/or as described
modulate expression of genes	below) and
involved in	immunodeficiencies (e.g., as
immunomodulatory functions.	described below). Preferred
 Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., leukemia,
NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
 modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
(including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
 66:1-10 (1998); Cullen and	dysproliferative disorders and
 Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
 31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
 al., J Exp Med 188:527-537	granulomatous disease,
(1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,

			Mast cells that may be used according to these assays are	suppression of immune reactions to transplanted
			publicly available (e.g., through the ATCC).	hypercoagulation, diabetes
			Exemplary human mast cells	mellitus, endocarditis,
			that may be used according to	meningitis, and Lyme Disease.
			these assays include the HMC-	
			1 cell line, which is an	
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HNTNI01	754	Activation of	This reporter assay measures	Highly preferred indication
		transcription	activation of the NFkB	includes allergy, asthma, and
		through NFKB	signaling pathway in HMC-1	rhinitis. Additional highly
		response element in	human mast cell line.	preferred indications include
		immune cells (such	Activation of NFkB in mast	infection (e.g., an infectious
		as mast cells).	cells has been linked to	disease as described below
			production of certain	under "Infectious Disease"),
			cytokines, such as IL-6 and IL-	and inflammation and
			9. Assays for the activation of	inflammatory disorders.
			transcription through the	Preferred indications include
			NFKB response element are	immunological and
			well-known in the art and may	hempatopoietic disorders (e.g.,
			be used or routinely modified	as described below under
			to assess the ability of	"Immune Activity", and
			polypeptides of the invention	"Blood-Related Disorders").
			(including antibodies and	Preferred indications also
			agonists or antagonists of the	include autoimmune diseases

i	invention) to regulate NFKB	(e.g., rheumatoid arthritis,
<u> </u>	transcription factors and	systemic lupus erythematosis,
<u> </u>	modulate expression of	multiple sclerosis and/or as
<u>. II</u>	immunomodulatory genes.	described below) and
<u>—</u>	Exemplary assays for	immunodeficiencies (e.g., as
	transcription through the	described below). Preferred
<u>Z</u>	NFKB response element that	indications also include
	may be used or rountinely	neoplastic diseases (e.g.,
 <u> </u>	modified to test NFKB-	leukemia, lymphoma,
re	response element activity of	melanoma, and/or as described
 <u>ă</u> ,	polypeptides of the invention	below under
	including antibodies and	"Hyperproliferative
 - T	agonists or antagonists of the	Disorders"). Preferred
 	invention) include assays	indications include neoplasms
	disclosed in Berger et al., Gene	and cancer, such as, for
 9	66:1-10 (1998); Cullen and	example, leukemia, lymphoma,
<u>~</u>	Malm, Methods in Enzymol	melanoma, and prostate,
 2	216:362-368 (1992); Henthorn	breast, lung, colon, pancreatic,
 	et al., Proc Natl Acad Sci USA	esophageal, stomach, brain,
 <u>×</u>	85:6342-6346 (1988); Stassen	liver, urinary tract cancers and
	et al, J Immunol 166(7):4391-8	as described below under
	(2001); and Marquardt and	"Hyperproliferative
 	Walker, J Allergy Clin	Disorders".
II	Immunol 105(3):500-5 (2000),	
 4	the contents of each of which	
<u> </u>	are herein incorporated by	
 7 J	reference in its entirety. Mast	
 	cells that may be used	
<u> </u>	according to these assays are	
 <u>d</u>	publicly available (e.g.,	
1	through the ATCC).	

			Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells	
HNTNI01	754	Activation of transcription through STAT6 response element in immune cells (such as mast cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element in immune cells (such as in the human HMC-1 mast cell line) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple general Examplements.	Highly preferred indications include allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications also include hematopoietic and immunological disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),
			assays for transcription through the STAT6 response element that may be used or routinely modified to test	autominute diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and

g s or ntion) d in 1-10 lm, 16:362- et al., A A aviya fasuda [asuda 1), the ich are ich are v v aviya 11), the ich are v ich are v ich are ich are v ich are v ich are ich are v ich are ich are v ich are ich are ich are ich are v ich are ich are i		
STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Sherman, Immunol Rev 179:48-56 (2001); Malaviya and Uckun, J Immunol 168:421-426 (2002); Masuda et al., J Biol Chem 275(38):29331-29337 (2000); and Masuda et al., J Biol Chem 276:26107-26113 (2001), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-	STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Sherman, Immunol Rev 179:48-56 (2001); Malaviya and Uckun, J Immunol 168:421-426 (2002); Masuda et al., J Biol Chem 275(38):29331-29337 (2000); and Masuda et al., J Biol Chem 276:26107-26113 (2001), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-	STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Sherman, Immunol Rev 179:48-56 (2001); Malaviya and Uckun, J Immunol 168:421-426 (2001); Masuda et al., J Biol Chem 275(38):29331-29337 (2000); and Masuda et al., J Biol Chem 276:26107-26113 (2001), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-

				immature human mast cell line established from the peripheral	organs and tissues, hemophilia, hypercoagulation, diabetes
				blood of a patient with mast	mellitus, endocarditis,
				cell leukemia, and exhibits	meningitis, and Lyme Disease.
				many characteristics of	
				immature mast cells.	
	HNTNI01	754	Activation of	This reporter assay measures	Highly preferred indication
			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
			response element in	human basophil cell line.	preferred indications include
			immune cells (such	Assays for the activation of	infection (e.g., an infectious
			as basophils).	transcription through the	disease as described below
				NFKB response element are	under "Infectious Disease"),
				well-known in the art and may	and inflammation and
				be used or routinely modified	inflammatory disorders.
-				to assess the ability of	Preferred indications include
				polypeptides of the invention	immunological and
				(including antibodies and	hempatopoietic disorders (e.g.,
				agonists or antagonists of the	as described below under
				invention) to regulate NFKB	"Immune Activity", and
				transcription factors and	"Blood-Related Disorders").
				modulate expression of	Preferred indications also
				immunomodulatory genes.	include autoimmune diseases
				Exemplary assays for	(e.g., rheumatoid arthritis,
				transcription through the	systemic lupus erythematosis,
				NFKB response element that	multiple sclerosis and/or as
				may be used or rountinely	described below) and
				modified to test NFKB-	immunodeficiencies (e.g., as
				response element activity of	described below). Preferred
				polypeptides of the invention	indications also include
				(including antibodies and	neoplastic diseases (e.g.,

			agonists or antagonists of the	leukemia, lymphoma,
				melanoma, and/or as described
			disclosed in Berger et al., Gene	below under
			66:1-10 (1998); Cullen and	"Hyperproliferative
			Malm, Methods in Enzymol	Disorders"). Preferred
			216:362-368 (1992); Henthorn	indications include neoplasms
			et al., Proc Natl Acad Sci USA	and cancer, such as, for
			85:6342-6346 (1988); Marone	example, leukemia, lymphoma,
			et al, Int Arch Allergy	melanoma, and prostate,
			Immunol 114(3):207-17	breast, lung, colon, pancreatic,
			(1997), the contents of each of	esophageal, stomach, brain,
			which are herein incorporated	liver, urinary tract cancers and
			by reference in its entirety.	as described below under
			Basophils that may be used	"Hyperproliferative
			according to these assays are	Disorders".
			publicly available (e.g.,	
			through the ATCC).	
			Exemplary human basophil	
 			cell lines that may be used	
			according to these assays	
			include Ku812, originally	
			established from a patient with	
			chronic myelogenous	
			leukemia. It is an immature	
			prebasophilic cell line that can	
			be induced to differentiate into	
			mature basophils.	
HNTNI01	754	SEAP in		
		Molt4/SRE		
HNTNI01	754	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include blood disorders (e.g.,

	through NFAT	Nuclear Factor of Activated T	as described below under
	response element in	cells (NFAT) response element	"Immune Activity", "Blood-
	immune cells (such	are well-known in the art and	Related Disorders", and/or
	as natural killer	may be used or routinely	"Cardiovascular Disorders").
	cells).	modified to assess the ability	Highly preferred indications
		of polypeptides of the	include autoimmune diseases
-		invention (including antibodies	(e.g., rheumatoid arthritis,
		and agonists or antagonists of	systemic lupus erythematosis,
		the invention) to regulate	multiple sclerosis and/or as
		NFAT transcription factors and	described below),
	-	modulate expression of genes	immunodeficiencies (e.g., as
		involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
		NFAT response element that	response. Additional highly
		may be used or routinely	preferred indications include
		modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
		invention) include assays	below under "Infectious
		disclosed in Berger et al., Gene	Disease"). Preferred
		66:1-10 (1998); Cullen and	indications include neoplastic
		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988);	"Hyperproliferative
		Aramburu et al., J Exp Med	Disorders"). Preferred
		182(3):801-810 (1995); De	indications include neoplasms

			Boer et al Int J Biochem Cell	and cancers, such as, for
			Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
			Fraser et al., Eur J Immunol	and prostate, breast, lung,
			29(3):838-844 (1999); and	colon, pancreatic, esophageal,
			Yeseen et al., J Biol Chem	stomach, brain, liver and
			268(19):14285-14293 (1993),	urinary cancer. Other preferred
			the contents of each of which	indications include benign
			are herein incorporated by	dysproliferative disorders and
			reference in its entirety. NK	pre-neoplastic conditions, such
			cells that may be used	as, for example, hyperplasia,
			according to these assays are	metaplasia, and/or dysplasia.
			publicly available (e.g.,	Preferred indications also
			through the ATCC).	include anemia, pancytopenia,
			Exemplary human NK cells	leukopenia, thrombocytopenia,
			that may be used according to	Hodgkin's disease, acute
			these assays include the NK-	lymphocytic anemia (ALL),
			YT cell line, which is a human	plasmacytomas, multiple
			natural killer cell line with	myeloma, Burkitt's lymphoma,
			cytolytic and cytotoxic	arthritis, AIDS, granulomatous
			activity.	disease, inflammatory bowel
				disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				asthma and allergy.
HNTNI01	754	SEAP in		
		NK16/STAT6		

immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and	inflammatory disorders. Highly preferred indications include blood disorders (e.g.,	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),	and infection (e.g., viral infections, tuberculosis, infections associated with	chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described	below under "Infectious Disease"). An additional preferred indication is	Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia	(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,
93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by	reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that	may be used according to meso assays are publicly available (e.g., through the ATCC).					
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sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,	nonketotic nyperglycemic-
sepsis neutro suppr reacti organ hemo diabe menii asthm	S S	
	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This stimulation of transcription is also somewhat glucose	dependent. Exemplary assays
	Regulation of transcription through the FAS promoter element in hepatocytes	
	755	
	HODDF13	

	that may be used or routinely	hyperosmolar coma,
	modified to test for FAS	
	promoter element activity (in	heart disease, atherosclerosis,
	hepatocytes) by polypeptides	microvascular disease,
	of the invention (including	hypertension, stroke, and other
	antibodies and agonists or	diseases and disorders as
	antagonists of the invention)	described in the
	include assays disclosed in	"Cardiovascular Disorders"
	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Acad Sci U.S.A., 97(8):3948-	-
	53 (2000); Roder, K., et al.,	described in the "Endocrine
	Eur J Biochem, 260(3):743-51	1 Disorders" section below),
	(1999); Oskouian B, et al.,	
	Biochem J, 317 (Pt 1):257-65	5 (e.g., diabetic retinopathy and
	(1996); Berger, et al., Gene	
	66:1-10 (1988); and, Cullen,	wound healing, and infection
	B., et al., Methods in Enzymol.	ol. (e.g., infectious diseases and
	216:362–368 (1992), the	-
	contents of each of which is	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety.	urinary tract and skin), carpal
-	Hepatocytes that may be used	tunnel syndrome and
	according to these assays, such	th Dupuytren's contracture).
	as H4IIE cells, are publicly	
	available (e.g., through the	indication is obesity and/or
	ATCC) and/or may be	complications associated with
	routinely generated.	obesity. Additional highly
	Exemplary hepatocytes that	preferred indications include
	may be used according to these	weight loss or alterna
	assays include rat liver	
	hepatoma cell line(s) inducible	le highly preferred indications are

			with glucocorticoids, insulin, or cAMP derivatives.	complications associated with insulin resistance.
HODDF13	755	Inhibition of squalene synthetase	Reporter Assay: construct contains regulatory and coding	
		gene transcription.	sequence of squalene	
			synthetase, the first specific	
			enzyme in the cholesterol	
			biosynthetic pathway. See	
			Jiang, et al., J. Biol. Chem.	
 			268:12818-128241(993), the	
			contents of which are herein	
			incorporated by reference in its	
			entirety. Cells were treated	
-			with SID supernatants, and	
			SEAP activity was measured	
			after 72 hours. HepG2 is a	
			human hepatocellular	
			carcinoma cell line (ATCC	
			HB-8065). See Knowles et al.,	
			Science. 209:497-9 (1980), the	
			contents of which are herein	
			incorporated by reference in its	
			entirety.	
HODDF13	755	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the GATA-3	include allergy, asthma, and
		through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and

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inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include
activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate GATA3 transcription	factors and modulate	expression of mast cell genes	important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Onant Riol 64: 563-571 (1999);
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			Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
			J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
			(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
			Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
			Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
			contents of each of which are	lymphoma, arthritis, AIDS,
			herein incorporated by	granulomatous disease,
			reference in its entirety. Mast	inflammatory bowel disease,
-			cells that may be used	sepsis, neutropenia,
			according to these assays are	neutrophilia, psoriasis,
			publicly available (e.g.,	suppression of immune
			through the ATCC).	reactions to transplanted
			Exemplary human mast cells	organs and tissues, hemophilia,
			that may be used according to	hypercoagulation, diabetes
			these assays include the HMC-	mellitus, endocarditis,
			1 cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
 HODDF13	755	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and

			activation of transcription	inflammatory disorders.
			through the Nuclear Factor of	Preferred indications also
			Activated T cells (NFAT)	include blood disorders (e.g.,
			response element are well-	as described below under
	_		known in the art and may be	"Immune Activity", "Blood-
			used or routinely modified to	Related Disorders", and/or
			assess the ability of	"Cardiovascular Disorders").
	_		polypeptides of the invention	Preferred indications include
			(including antibodies and	autoimmune diseases (e.g.,
		-	agonists or antagonists of the	rheumatoid arthritis, systemic
_	-		invention) to regulate NFAT	lupus erythematosis, multiple
			transcription factors and	sclerosis and/or as described
			modulate expression of genes	below) and
-			involved in	immunodeficiencies (e.g., as
		-	immunomodulatory functions.	described below). Preferred
			Exemplary assays for	indications include neoplastic
	_		transcription through the	diseases (e.g., leukemia,
-		_	NFAT response element that	lymphoma, melanoma,
	_		may be used or routinely	prostate, breast, lung, colon,
			modified to test NFAT-	pancreatic, esophageal,
			response element activity of	stomach, brain, liver, and
_	_		polypeptides of the invention	urinary tract cancers and/or as
			(including antibodies and	described below under
		_	agonists or antagonists of the	"Hyperproliferative
			invention) include assays	Disorders"). Other preferred
			disclosed in Berger et al., Gene	indications include benign
		-	66:1-10 (1998); Cullen and	dysproliferative disorders and
	_		Malm, Methods in Enzymol	pre-neoplastic conditions, such
- 7	_		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
			et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
			85:6342-6346 (1988); De Boer	Preferred indications include

2	Highly preferred indications Include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include
et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Ali et al., J Immunol 165(12):7215-7223 (2000); Hutchinson and McCloskey, J Biol Chem 270(27):16333-16338 (1995), and Turner et al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells
	755
	HODDF13

inflammation and	inflammatory disorders,	immunological disorders,	neoplastic disorders (e.g.	cancer/tumorigenesis), and	cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.					
(including antibodies and	agonists or antagonists of the	invention) to regulate VCAM	expression. For example,	FMAT may be used to meaure	the upregulation of cell surface	VCAM-1 expresssion in	endothelial cells. Endothelial	cells are cells that line blood	vessels, and are involved in	functions that include, but are	not limited to, angiogenesis,	vascular permeability, vascular	tone, and immune cell	extravasation. Exemplary	endothelial cells that may be	used according to these assays	include human umbilical vein	endothelial cells (HUVEC),	which are available from	commercial sources. The	expression of VCAM	(CD106), a membrane-	associated protein, can be	upregulated by cytokines or	other factors, and contributes	to the extravasation of	lymphocytes, leucocytes and	other immune cells from blood	vessels; thus VCAM	expression plays a role in
(HUVEC))													,					-												
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			A highly preferred embodiment of the invention
promoting immune and inflammatory responses.		Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours. LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its entirety.	IL-6 FMAT. IL-6 is produced by T cells and has strong
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	Activation of Transcription	Production of IL-6
	755	755	756
	HODDF13	HODDF13	HODDN92

includes a method for	stimulating (e.g., increasing)	IL-6 production. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting (e.g.,	reducing) IL-6 production. A	highly preferrred indication is	the stimulation or enhancement	of mucosal immunity. Highly	preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a
effects on B cells. IL-6	participates in IL-4 induced	IgE production and increases	IgA production (IgA plays a	role in mucosal immunity).	IL-6 induces cytotoxic T cells.	Deregulated expression of IL-6	has been linked to autoimmune	disease, plasmacytomas,	myelomas, and chronic	hyperproliferative diseases.	Assays for immunomodulatory	and differentiation factor	proteins produced by a large	variety of cells where the	expression level is strongly	regulated by cytokines, growth	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of
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		cytokines such as II6 and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
		may be used or routinely	disorders.Additional highly
	٠	modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
-		polypeptides of the invention	neoplastic diseases (e.g.,
		including antibodies and	myeloma, plasmacytoma,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
		be used according to these	indications include benign
		assays may be isolated using	dysproliferative disorders and
		techniques disclosed herein or	pre-neoplastic conditions, such
		otherwise known in the art.	as, for example, hyperplasia,
		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,

				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
-					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
	-				organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
	-				An additonal preferred
	,				indication is infection (e.g., an
-					infectious disease as described
_					below under "Infectious
					Disease").
HODDN92	26No	756	Production of	MCP-1 FMAT. Assays for	A highly preferred
			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred
				cells are well known in the art	embodiment of the invention
				and may be used or routinely	includes a method for
				modified to assess the ability	inhibiting (e.g., reducing)
	-			of polypeptides of the	MCP-1 production. A highly
				invention (including antibodies	preferred indication is

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infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	Iymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,
and agonists or antagonists of	the invention) to mediate	immunomodulation, induce	chemotaxis, and modulate	immune cell activation.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of cell	surface markers, such as	monocyte chemoattractant	protein (MCP), and the	activation of monocytes and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); and	Verhasselt et al., J Immunol	158:2919-2925 (1997), the	contents of each of which are
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				herein incorporated by	neutrophilia, psoriasis,
				reference in its entirety.	suppression of immune
-				Human dendritic cells that may	reactions to transplanted
				be used according to these	organs and tissues,
				assays may be isolated using	hemophilia, hypercoagulation,
				techniques disclosed herein or	diabetes mellitus, endocarditis,
				otherwise known in the art.	meningitis (bacterial and
_				Human dendritic cells are	viral), Lyme Disease, asthma,
				antigen presenting cells in	and allergy Preferred
				suspension culture, which,	indications also include
				when activated by antigen	neoplastic diseases (e.g.,
				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
				and functional activities.	"Hyperproliferative
					Disorders"). Highly preferred
	_				indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
·					liver, and urinary cancer. Other
					preferred indications include
_	-				benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HODDN92	952	Production of	MIP-1alpha FMAT. Assays	A highly preferred
			MIP1alpha	for immunomodulatory	embodiment of the invention
				proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.

known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention preferred indications include and	3-3-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1	3-3-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1	3-3-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1
cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate invention) to mediate invention, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemotics, such as macrophage inflammatory protein I alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-

plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,	asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of	by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.

	HODDN92	756	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
			promoter element	known in the art and may be	indication is a complication
_			in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
		·		(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the FAS	diseases and disorders as
				promoter element in a reporter	described in the "Renal
				construct and to regulate	Disorders" section below),
		-		transcription of FAS, a key	diabetic neuropathy, nerve
				enzyme for lipogenesis. FAS	disease and nerve damage
				promoter is regulated by many	(e.g., due to diabetic
				transcription factors including	neuropathy), blood vessel
				SREBP. Insulin increases FAS	blockage, heart disease, stroke,
				gene transcription in livers of	impotence (e.g., due to diabetic
				diabetic mice. This	neuropathy or blood vessel
		2-50		stimulation of transcription is	blockage), seizures, mental
				also somewhat glucose	confusion, drowsiness,
				dependent. Exemplary assays	nonketotic hyperglycemic-
				that may be used or routinely	hyperosmolar coma,
				modified to test for FAS	cardiovascular disease (e.g.,
				promoter element activity (in	heart disease, atherosclerosis,
				hepatocytes) by polypeptides	microvascular disease,
				of the invention (including	hypertension, stroke, and other
				antibodies and agonists or	diseases and disorders as
				antagonists of the invention)	described in the
				include assays disclosed in	"Cardiovascular Disorders"
				Xiong, S., et al., Proc Natl	section below), dyslipidemia,

				Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
				53 (2000); Roder, K., et al.,	described in the "Endocrine
				Eur J Biochem, 260(3):743-51	Disorders" section below),
				(1999); Oskouian B, et al.,	neuropathy, vision impairment
				Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
				(1996); Berger, et al., Gene	blindness), ulcers and impaired
				66:1-10 (1988); and, Cullen,	wound healing, and infection
				B., et al., Methods in Enzymol.	(e.g., infectious diseases and
				216:362–368 (1992), the	disorders as described in the
				contents of each of which is	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety.	urinary tract and skin), carpal
				Hepatocytes that may be used	tunnel syndrome and
				according to these assays, such	Dupuytren's contracture).
				as H4IIE cells, are publicly	An additional highly preferred
				available (e.g., through the	indication is obesity and/or
				ATCC) and/or may be	complications associated with
				routinely generated.	obesity. Additional highly
				Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
				assays include rat liver	weight gain. Aditional
				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HODDN92	756	Activation of	This reporter assay measures	Highly preferred indications
			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
_			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and

		_								_											-							_		
inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.
production. Assays for the	activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate GATA3 transcription	factors and modulate	expression of mast cell genes	important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp
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	-				-																									
										_																	_			

			Quant Biol 64:563-571 (1999);	Preferred indications include
			Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
			J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
			(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
			Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
			Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
		-	contents of each of which are	lymphoma, arthritis, AIDS,
			herein incorporated by	granulomatous disease,
-			reference in its entirety. Mast	inflammatory bowel disease,
			cells that may be used	sepsis, neutropenia,
			according to these assays are	neutrophilia, psoriasis,
			publicly available (e.g.,	suppression of immune
			through the ATCC).	reactions to transplanted
			Exemplary human mast cells	organs and tissues, hemophilia,
			that may be used according to	hypercoagulation, diabetes
			these assays include the HMC-	mellitus, endocarditis,
			1 cell line, which is an	meningitis, and Lyme Disease.
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HODDN92	756	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the NFAT	include allergy, asthma, and
		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and

modication Accove for the inflammation and	 r of	response element are well- as described below under	known in the art and may be 'Immune Activity", "Blood-	used or routinely modified to Related Disorders", and/or	assess the ability of "Cardiovascular Disorders").	tion	(including antibodies and autoimmune diseases (e.g.,	agonists or antagonists of the rheumatoid arthritis, systemic	invention) to regulate NFAT lupus erythematosis, multiple	transcription factors and sclerosis and/or as described	modulate expression of genes below) and	involved in immunodeficiencies (e.g., as	immunomodulatory functions. described below). Preferred	Exemplary assays for indications include neoplastic	transcription through the diseases (e.g., leukemia,	NFAT response element that lymphoma, melanoma,	may be used or routinely prostate, breast, lung, colon,	modified to test NFAT- pancreatic, esophageal,	response element activity of stomach, brain, liver, and	polypeptides of the invention urinary tract cancers and/or as	(including antibodies and described below under	agonists or antagonists of the "Hyperproliferative	invention) include assays Disorders"). Other preferred	disclosed in Berger et al., Gene indications include benign	66:1-10 (1998); Cullen and dysproliferative disorders and	Malm, Methods in Enzymol pre-neoplastic conditions, such	

HODDN92 756 Activation of	Le L	anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease,
756		leukopenia, thrombocytopenia, leukemias, Hodgkin's disease,
756		leukemias, Hodgkin's disease,
756		``
756		acute lymphocytic anemia
756		(ALL), plasmacytomas,
756		multiple myeloma, Burkitt's
756		lymphoma, arthritis, AIDS,
756	al., J Exp Med 188:527-537	granulomatous disease,
756	دسا	inflammatory bowel disease,
756	which are herein incorporated s	sepsis, neutropenia,
756	by reference in its entirety.	neutrophilia, psoriasis,
756	Mast cells that may be used s	suppression of immune
756	according to these assays are	reactions to transplanted
756		organs and tissues, hemophilia,
756		hypercoagulation, diabetes
756	Exemplary human mast cells n	mellitus, endocarditis,
756	that may be used according to n	meningitis, and Lyme Disease.
756	these assays include the HMC-	
756	1 cell line, which is an	
756	immature human mast cell line	
756	established from the peripheral	
756	blood of a patient with mast	
756	cell leukemia, and exhibits	
756	many characteristics of	
126	immature mast cells.	
	tion of Kinase assay. JNK and p38	A highly preferred
	Endothelial Cell kinase assays for signal e	embodiment of the invention
p38 or JNK	transduction that regulate cell	includes a method for
Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
	apoptosis are well known in	growth. An alternative highly

. Les E		the art and may be used or	preferred embodiment of the
s of nod any to on) to on) to on on on on on on on on on on		routinely modified to assess	invention includes a method
on) to nd ays or JNK Sthe odies s of et to 101- Exp Hem Mol (99); ich		the shility of nolynearides of	for inhibiting on dotholist coll
on) to nd ays or JNK Sthe odies s of et to 101- Exp Hem Mol Mol 99); ich		 use ability of polypeptides of	tor infilibiting endotherial cell
on) to nd ays or JNK JNK s of et 1101- Exp Hem Mol Mol Mol		the invention (including	growth. A highly preferred
on) to nd ays or JNK JNK et 101- Exp Hem Mol Mol (99); ich		antibodies and agonists or	embodiment of the invention
ays or JNK the odies s of et 101- Exp md Mol Mol 99); ich	-	antagonists of the invention) to	includes a method for
ays or JNK JNK Sthe odies s of et them hem Mol Mol 99; ich		promote or inhibit cell	stimulating endothelial cell
ays or JNK JNK che odies s of et tot l101- Exp Hem hem ho he md Mol 99);	-	 proliferation, activation, and	proliferation. An alternative
or JNK Sthe odies s of tet 101- Exp Exp hem Mol Mol 99); ich		apoptosis. Exemplary assays	highly preferred embodiment
JNK The odies s of et et Exp Exp Mol Mol (99); ich		for JNK and p38 kinase	of the invention includes a
JNK the odies s of et and them (hem); md Mol (99); ich be		 activity that may be used or	method for inhibiting
s of s odies s of et et Exp Exp (Mol Mol 99); ich		routinely modified to test JNK	endothelial cell proliferation.
the odies s of et 1101-Exp hem (99); ich	-	and p38 kinase-induced	A highly preferred
s of s of et 101- Exp hem hem Mol (99); ich		activity of polypeptides of the	embodiment of the invention
e et 1101- Exp Exp withem Mol (99); ich	-	 invention (including antibodies	includes a method for
et 101- Exp Exp hem (9); ich		and agonists or antagonists of	stimulating apoptosis of
eet 101- 101- Exp hem hem Mol (99); ich		the invention) include the	endothelial cells. An
Exp Exp (hem them /); (hem //0); (ich be		assays disclosed in Forrer et	alternative highly preferred
Exp hem hem md md Mol ich ich		al., Biol Chem 379(8-9):1101-	embodiment of the invention
them (); und (Mol (99); ich (be		1110 (1998); Gupta et al., Exp	includes a method for
them (); mid (Mol (99)); ich (be		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
); md Mol (99); ich		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
und Mol (9); ich	-	Soc Symp 64:29-48 (1999);	A highly preferred
md (Mol ich be		Chang and Karin, Nature	embodiment of the invention
Mol (9);	-	 410(6824):37-40 (2001); and	includes a method for
(9); ich be		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
ich be		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
þ		 the contents of each of which	alternative highly preferred
ay be		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
1		Endothelial cells that may be	inhibiting (e.g., decreasing) the

arrange aget of anibacoge beau	notiving of and/on
asca according to these assays	
are publicly available (e.g.,	mactivating endothelial cells.
through the ATCC).	A highly preferred
Exemplary endothelial cells	embodiment of the invention
that may be used according to	includes a method for
these assays include human	stimulating angiogenisis. An
umbilical vein endothelial cells	alternative highly preferred
(HUVEC), which are	embodiment of the invention
endothelial cells which line	includes a method for
venous blood vessels, and are	inhibiting angiogenesis. A
involved in functions that	highly preferred embodiment
include, but are not limited to,	of the invention includes a
angiogenesis, vascular	method for reducing cardiac
permeability, vascular tone,	hypertrophy. An alternative
and immune cell extravasation.	highly preferred embodiment
	of the invention includes a
	method for inducing cardiac
	hypertrophy. Highly
	preferred indications include
	neoplastic diseases (e.g., as
	described below under
	"Hyperproliferative
	Disorders"), and disorders of
	the cardiovascular system
	(e.g., heart disease, congestive
	heart failure, hypertension,
	aortic stenosis,
	cardiomyopathy, valvular
	regurgitation, left ventricular
	dysfunction, atherosclerosis
	and atherosclerotic vascular

disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or anoiogenic	disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves such as of the	arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly	preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s	sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma,
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telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such
indications include benign dysproliferative disorders and pre-neoplastic conditions, such
dysproliferative disorders and pre-neoplastic conditions, such
pre-neoplastic conditions, such
as, for example, hyperplasia,
metaplasia, and/or dysplasia.
Highly preferred indications
also include arterial disease,
such as, atherosclerosis,
hypertension, coronary artery
disease, inflammatory
vasculitides, Reynaud's
disease and Reynaud"s
phenomenom, aneurysms,
restenosis; venous and
lymphatic disorders such as
thrombophlebitis,

lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas
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				heart disease, cardiac arrest,
				heart valve disease, and
				vascular disease.
				Preferred indications include
				blood disorders (e.g., as
				described below under
				"Immune Activity", "Blood-
				Related Disorders", and/or
				"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
			1	described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
-				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HODFN71	757	Inhibition of	Reporter Assay: construct	
		squalene synthetase	contains regulatory and coding	
		gene transcription.	sequence of squarene	
			אווווכנשטלי, וווי דוויטן ארטיווויט	
			enzyme in the cholesterol	
			biosynthetic pathway. See	

			Jiang, et al., J. Biol. Chem. 268:12818-128241/9933, the	
			contents of which are herein	
			incorporated by reference in its	
			entirety. Cells were treated	
			with SID supernatants, and	
			SEAP activity was measured	
			after 72 hours. HepG2 is a	
			human hepatocellular	
			carcinoma cell line (ATCC	
-			HB-8065). See Knowles et al.,	
			Science. 209:497-9 (1980), the	
			contents of which are herein	
			incorporated by reference in its	
			entirety.	
HODFN71	151	IL-2 in Human T-		
		cell 293T		
HODFN71	151	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	highly preferred embodiment
			the ability of polypeptides of	of the invention includes a
			the invention (including	method for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth and upregulate the	Activity", "Blood-Related

Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, Crohn"s disease, multiple	sclerosis and/or as described below). immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	Iymphoma, melanoma, glioma
function of growth-related genes in many cell types. Exemplary assays for	transcription through the SRE that may be used or routinely	modified to test SRE activity of the polypeptides of the	invention (including antibodies and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm Mathods in Engaged	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety.	Human T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the JURKAT	cell line, which is a suspension	culture of leukemia cells that
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(e.g., malignant glioma), solid tumors, and prostate, breast	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication
produce IL-2 when stimulated.																													
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is infection (e.g., an infectious disease as described below under "Infectious Disease").		Accase for the activation of Highly preferred indications			Nuclear Factor of Activated T as described below under	cells (NFAT) response element "Immune Activity", "Blood-		may be used or routinely Cardiovascular Disorders").	modified to assess the ability Highly preferred indications	es of the include autoimmune diseases	invention (including antibodies (e.g., rheumatoid arthritis,	and agonists or antagonists of systemic lupus erythematosis,	the invention) to regulate multiple sclerosis and/or as	rs and	modulate expression of genes immunodeficiencies (e.g., as	described below), boosting a T	immunomodulatory functions. cell-mediated immune	says for response, and suppressing a T	transcription through the cell-mediated immune	NFAT response element that response. Additional highly	or routinely preferred indications include	est NFAT- inflammation and	response element activity of inflammatory disorders. An	polypeptides of the invention additional highly preferred	(including antibodies and indication is infection (e.g., an	agonists or antagonists of the infectious disease as described	invention) include assays below under "Infectious	
	SEAP in Molt4/SRE	J.		<u> </u>	through NFAT Nuclear Fac	nt in	immune cells (such are well-kno	as natural killer may be used	cells). modified to	of polypeptides of the	invention (i	and agonist	the inventio	NFAT trans	modulate ex	involved in	omonumi	Exemplary assays for	transcription	NFAT respo	may be used or routinely	modified to test NFAT-	response ele	polypeptide	(including a	agonists or a	invention) i	
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	HODFN71	HODEN71	I I I I I I I I I I I I I I I I I I I																									

			66:1-10 (1998); Cullen and	indications include neoplastic
			Malm. Methods in Enzymol	diseases (e.g., leukemia,
			216:362-368 (1992); Henthorn	lymphoma, and/or as described
			et al., Proc Natl Acad Sci USA	below under
			85:6342-6346 (1988);	"Hyperproliferative
			Aramburu et al., J Exp Med	Disorders"). Preferred
			182(3):801-810 (1995); De	indications include neoplasms
	•		Boer et al., Int J Biochem Cell	and cancers, such as, for
			Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
			Fraser et al., Eur J Immunol	and prostate, breast, lung,
			29(3):838-844 (1999); and	colon, pancreatic, esophageal,
			Yeseen et al., J Biol Chem	stomach, brain, liver and
			268(19):14285-14293 (1993),	urinary cancer. Other preferred
			the contents of each of which	indications include benign
			are herein incorporated by	dysproliferative disorders and
			reference in its entirety. NK	pre-neoplastic conditions, such
			cells that may be used	as, for example, hyperplasia,
			according to these assays are	metaplasia, and/or dysplasia.
			publicly available (e.g.,	Preferred indications also
-			through the ATCC).	include anemia, pancytopenia,
			Exemplary human NK cells	leukopenia, thrombocytopenia,
			that may be used according to	Hodgkin's disease, acute
			these assays include the NK-	lymphocytic anemia (ALL),
			YT cell line, which is a human	plasmacytomas, multiple
			natural killer cell line with	myeloma, Burkitt's lymphoma,
		-	cytolytic and cytotoxic	arthritis, AIDS, granulomatous
			activity.	disease, inflammatory bowel
				disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted

				organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HODFN71	757	Activation of transcription	Assays for the activation of transcription through the	A preferred embodiment of the invention includes a
		through serum response element in	Serum Response Element (SRE) are well-known in the	method for inhibiting (e.g., reducing) TNF alpha
		immune cells (such as natural killer	art and may be used or routinely modified to assess	production. An alternative highly preferred embodiment
		cells).	the ability of polypeptides of	of the invention includes a method for stimulating (e.g
			antibodies and agonists or	increasing) TNF alpha
 =			antagonists of the invention) to	production. Preferred indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth and upregulate the	Activity", "Blood-Related
			genes in many cell types.	"Cardiovascular Disorders"),
			Exemplary assays for	Highly preferred indications
			transcription through the SRE	include autoimmune diseases
			that may be used or routinely	(e.g., rheumatoid arthritis,
			modified to test SRE activity	systemic lupus erythematosis,
			of the polypeptides of the	Crohn"s disease, multiple
			invention (including antibodies	scierosis and/or as described below) imminodeficiencies
			the invention) include assays	(e.g., as described below),
	,		disclosed in Berger et al., Gene	boosting a T cell-mediated
			66:1-10 (1998); Cullen and	immune response, and

suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in patients with rheumatoid	arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below	Disorders"). Additionally, highly preferred indications	include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma). solid	tumors, and prostate, breast, lung, colon, pancreatic,	liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia.
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g.,	Exemplary T cells that may be used according to these assays	include the NK-YT cell line, which is a human natural killer	cell line with cytolytic and cytotoxic activity.				

Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention
		Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of
	SEAP in NK16/STAT6	Activation of transcription through CD28 response element in immune cells (such as T-cells).
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	HODFN71	HODFN71

includes a method for inhibiting T cell proliferation. A highly preferred	embodiment of the invention	includes a method for	atternative highly preferred	embodiment of the invention	includes a method for	inhibiting the activation of	and/or inactivating T cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	IL-2 production. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as
polypeptides of the invention (including antibodies and	invention) to stimulate IL-2	expression in T cells.	transcription through the CD28	response element that may be	used or routinely modified to	test CD28-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are
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	ildud	publicly available (e.g.,	described below), boosting a T
	thron	through the ATCC).	cell-mediated immune
	Exem	F cells that	response, and suppressing a T
	may	se	cell-mediated immune
	assay	assays include the SUPT cell	response. Highly preferred
	line,	line, which is a suspension	indications include neoplastic
	cultu	culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
	respo	responsive T cells.	cell carcinoma, leukemia,
			lymphoma, and/or as described
			below under
			"Hyperproliferative
			Disorders"). Highly preferred
			indications include neoplasms
			and cancers, such as, for
-		•	example, melanoma (e.g.,
		•	metastatic melanoma), renal
			cell carcinoma (e.g., metastatic
	-		renal cell carcinoma),
			leukemia, lymphoma (e.g., T
		•	cell lymphoma), and prostate,
		,	breast, lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
-			example, hyperplasia,
			metaplasia, and/or dysplasia.
			A highly preferred indication
			includes infection (e.g.,

		AIDS tuber	AIDS tuberculosis infections
		Con 'Corry'	culosis, misculons
		associated v	associated with granulomatous
		disease, and	disease, and osteoporosis,
		and/or as de	and/or as described below
		nnder "Infe	under "Infectious Disease"). A
		highly prefe	highly preferred indication is
		AIDS. Ad	AIDS. Additional highly
		preferred in	preferred indications include
		suppression of immune	of immune
	-	reactions to	reactions to transplanted
		organs and/	organs and/or tissues, uveitis,
		psoriasis, ar	psoriasis, and tropical spastic
		paraparesis.	Preferred
		indications	indications include blood
		disorders (e	disorders (e.g., as described
		below under "Immune	. "Immune
		Activity", "	Activity", "Blood-Related
		Disorders", and/or	and/or
		"Cardiovasc	"Cardiovascular Disorders").
-		Preferred in	Preferred indications also
		include aner	include anemia, pancytopenia,
		leukopenia,	leukopenia, thrombocytopenia,
		Hodgkin's c	Hodgkin's disease, acute
		lymphocytic	lymphocytic anemia (ALL),
		plasmacytor	plasmacytomas, multiple
		myeloma, B	myeloma, Burkitt's lymphoma,
		arthritis, gra	arthritis, granulomatous
		disease, infl	disease, inflammatory bowel
		disease, sep	disease, sepsis, neutropenia,
		neutrophilia	neutrophilia, hemophilia,
		hypercoagu	hypercoagulation, diabetes

				mellitus, endocarditis,
	,			meningitis, Lyme Disease,
				asthma and allergy.
HODFN71	757	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include inflammation and
	_	through NFKB	NFKB response element are	inflammatory disorders.
		response element in	well-known in the art and may	Highly preferred indications
	_	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
		as T-cells).	to assess the ability of	as described below under
_			polypeptides of the invention	"Immune Activity", "Blood-
	_		including antibodies and	Related Disorders", and/or
			agonists or antagonists of the	"Cardiovascular Disorders").
 			invention) to regulate NFKB	Highly preferred indications
			transcription factors and	include autoimmune diseases
 	170.00		modulate expression of	(e.g., rheumatoid arthritis,
 			immunomodulatory genes.	systemic lupus erythematosis,
			Exemplary assays for	multiple sclerosis and/or as
			transcription through the	described below), and
	~		NFKB response element that	immunodeficiencies (e.g., as
_			may be used or rountinely	described below). An
 	-		modified to test NFKB-	additional highly preferred
			response element activity of	indication is infection (e.g.,
 			polypeptides of the invention	AIDS, and/or an infectious
			(including antibodies and	disease as described below
			agonists or antagonists of the	under "Infectious Disease").
 			invention) include assays	Highly preferred indications
 			disclosed in Berger et al., Gene	include neoplastic diseases
		-	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
			Malm, Methods in Enzymol	lymphoma, and/or as described
 			216:362-368 (1992); Henthorn	below under
			et al., Proc Natl Acad Sci USA	"Hyperproliferative

				reactions to transplanted organs, asthma and allergy.
HODGE68	758	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
_		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	highly preferred embodiment
			the ability of polypeptides of	of the invention includes a
			the invention (including	method for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth and upregulate the	Activity", "Blood-Related
			function of growth-related	Disorders", and/or
			genes in many cell types.	"Cardiovascular Disorders"),
			Exemplary assays for	Highly preferred indications
			transcription through the SRE	include autoimmune diseases
			that may be used or routinely	(e.g., rheumatoid arthritis,
			modified to test SRE activity	systemic lupus erythematosis,
_			of the polypeptides of the	Crohn"s disease, multiple
			invention (including antibodies	sclerosis and/or as described
_			and agonists or antagonists of	below), immunodeficiencies
			the invention) include assays	(e.g., as described below),
			disclosed in Berger et al., Gene	boosting a T cell-mediated
	412.33		66:1-10 (1998); Cullen and	immune response, and
			Malm, Methods in Enzymol	suppressing a T cell-mediated
			216:362-368 (1992); Henthorn	immune response. Additional
			et al. Proc Natl Acad Sci USA	highly preferred indications

Benson include inflammation and b):3862- inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly porated preferred indication is sepsis.		lls that Iymphoma, melanoma, glioma mulated. (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute
85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated	by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension	culture of leukemia cells that produce IL-2 when stimulated.

·	•			lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel. disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
НОЕDВ32	759	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious

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under "Infectious Disease"). Preferred indications include	Frederica marcanons morace	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute		plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transminanted
invention) to mediate	chemotaxis and modulate T	cell differentiation. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	[mmiino] 158.2010_2025
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			(1997); and Nardelli et al., J	organs and tissues, hemophilia,
			Leukoc Biol 65:822-828	hypercoagulation, diabetes
			(1999), the contents of each of	mellitus, endocarditis,
			which are herein incorporated	meningitis, Lyme Disease,
			by reference in its entirety.	asthma, and allergy.
			Human dendritic cells that may	Preferred indications also
			be used according to these	include neoplastic diseases
			assays may be isolated using	(e.g., leukemia, lymphoma,
			techniques disclosed herein or	and/or as described below
			otherwise known in the art.	under "Hyperproliferative
			Human dendritic cells are	Disorders"). Highly preferred
			antigen presenting cells in	indications include neoplasms
			suspension culture, which,	and cancers, such as, leukemia,
			when activated by antigen	lymphoma, prostate, breast,
			and/or cytokines, initiate and	lung, colon, pancreatic,
			upregulate T cell proliferation	esophageal, stomach, brain,
			and functional activities.	liver, and urinary cancer. Other
				preferred indications include
				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
HOEDB32	759	Production of TNF	TNFa FMAT. Assays for	A highly preferred
		alpha by dendritic	immunomodulatory proteins	embodiment of the invention
		cells	produced by activated	includes a method for
			macrophages, T cells,	inhibiting (e.g., decreasing)
-			fibroblasts, smooth muscle,	TNF alpha production. An
			and other cell types that exert a	alternative highly preferred
			wide variety of inflammatory	embodiment of the invention
			and cytotoxic effects on a	includes a method for

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stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below
variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Verhasselt et al Eur J
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90 under "Hyperproliferative Disorders"). Additionally, 93 highly preferred indications		<u> </u>	ay	Ing benign dysproliterative in or disorders and pre-neoplastic t. conditions, such as, for		Preferred indications include anemia, pancytopenia,		lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia,	neutrophilia, psoriasis, suppression of immune reactions to transplanted	organs and tissues
Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593	(1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J	Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety	Human dendritic cells that may be used according to these	assays may be isolated using techniques disclosed herein or otherwise known in the art.	Human dendritic cells are antigen presenting cells in	suspension culture, which, when activated by antigen	and/or cytokines, initiate and upregulate T cell proliferation	and functional activities.			

					hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HO	HOEDB32	759	MCP-1 in Eol-1		
OH HO	HOEDB32	759	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
-			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
-				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn's disease, multiple

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sclerosis and/or as described below), immunodeficiencies (e.g., as described below),		immune response. Additional highly preferred indications	include inflammation and inflammatory disorders, and	treating joint damage in patients with rheumatoid	arthritis. An additional highly	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliterative Disorders"). Additionally,	highly preferred indications	include neoplasms and		leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include
invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-	3873 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of	which are nerein incorporated by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC). Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.						
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benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious	disease as described below under "Infectious Disease").	A highly preferred indication is allergy. Another highly preferred
		Assays for the activation of transcription through the Signal Transducers and
		Activation of transcription through STAT6
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response element in minimum cells (such well-known in the art and may well-known in the art and may be used or routinely modified inflammation and inflammation and no assess the ability of inflammation and inflammation and inflammation and probypeptides of the invention) to regulate STAT6 invention) to regulate STAT6 invention) to regulate STAT6 inflammation include assays for transcription factors and multiple genes. Exemplary assays for transcription assays for transcription assays for transcription assays for transcription and that may be used or cutimely modified to test STAT6 response element antipodies and agonists or antipodies and agonists of the invention) including antipodies and agonists of the invention) include assays disclosed in mununodeficiencies (e.g., antipodies and agonists of the invention) include assays disclosed in mununodeficiencies (e.g., include assays disclosed in munununumunumunumunumunumunumunumunumu	Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362- 368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538
response element in immune cells (such as T-cells).	response element in immune cells (such as T-cells).

			1523 (2000); Curiel et al., Eur	stomach, brain, liver and
		-	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
			(1997); and Masuda et al., J	indications include benign
			Biol Chem 275(38):29331-	dysproliferative disorders and
			29337 (2000), the contents of	pre-neoplastic conditions, such
			each of which are herein	as, for example, hyperplasia,
			incorporated by reference in its	metaplasia, and/or dysplasia.
			entirety. T cells that may be	Preferred indications include
			used according to these assays	anemia, pancytopenia,
			are publicly available (e.g.,	leukopenia, thrombocytopenia,
			through the ATCC).	Hodgkin's disease, acute
			Exemplary T cells that may be	lymphocytic anemia (ALL),
			used according to these assays	plasmacytomas, multiple
			include the SUPT cell line,	myeloma, Burkitt's lymphoma,
			which is a suspension culture	arthritis, AIDS, granulomatous
-			of IL-2 and IL-4 responsive T	disease, inflammatory bowel
			cells.	disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additional preferred
				indication is infection (e.g., an
				infectious disease as described
				below under "Infectious
				Disease").
НОҒМQ33	092	Regulation of	Assays for the regulation of	A highly preferred indication is diabetes mellitus. An
		Viaulity and	viability and promistation of	13 diductos monitors, 1 m

	proliferation of	cells in vitro are well-known in	additional highly preferred
-	pancreatic beta	the art and may be used or	
	cells.	routinely modified to assess	associated with diabetes (e.g.,
		the ability of polypeptides of	diabetic retinopathy, diabetic
		the invention (including	nephropathy, kidney disease
		antibodies and agonists or	(e.g., renal failure,
		antagonists of the invention) to	nephropathy and/or other
		regulate viability and	diseases and disorders as
		proliferation of pancreatic beta	described in the "Renal
	-	cells. For example, the Cell	Disorders" section below),
		Titer-Glo luminescent cell	diabetic neuropathy, nerve
		viability assay measures the	disease and nerve damage
		number of viable cells in	(e.g., due to diabetic
-		culture based on quantitation	neuropathy), blood vessel
-		of the ATP present which	blockage, heart disease, stroke,
		signals the presence of	impotence (e.g., due to diabetic
-		metabolically active cells.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
-		test regulation of viability and	nonketotic hyperglycemic-
		proliferation of pancreatic beta	hyperosmolar coma,
		cells by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ohtani KI, et al.,	diseases and disorders as
		Endocrinology, 139(1):172-8	described in the
		(1998); Krautheim A, et al,	"Cardiovascular Disorders"
		Exp Clin Endocrinol Diabetes,	section below), dyslipidemia,
		107 (1):29-34 (1999), the	endocrine disorders (as
		contents of each of which is	described in the "Endocrine

			herein incorporated by	Disorders" section below).
			reference in its entirety.	neuropathy, vision impairment
			Pancreatic cells that may be	(e.g., diabetic retinopathy and
			used according to these assays	blindness), ulcers and impaired
			are publicly available (e.g.,	wound healing, and infection
			through the ATCC) and/or	(e.g., infectious diseases and
-			may be routinely generated.	disorders as described in the
			Exemplary pancreatic cells that	"Infectious Diseases" section
			may be used according to these	below, especially of the
			assays include HITT15 Cells.	urinary tract and skin), carpal
			HITT15 are an adherent	tunnel syndrome and
			epithelial cell line established	Dupuytren's contracture). An
			from Syrian hamster islet cells	additional highly preferred
			transformed with SV40. These	indication is obesity and/or
			cells express glucagon,	complications associated with
			somatostatin, and	obesity. Additional highly
			glucocorticoid receptors. The	preferred indications include
			cells secrete insulin, which is	weight loss or alternatively,
			stimulated by glucose and	weight gain. Additional highly
			glucagon and suppressed by	preferred indications are
			somatostatin or	complications associated with
			glucocorticoids. ATTC# CRL-	insulin resistance.
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
НОҒМQ33	092	SEAP in Molt4/SRE		
HOFMT75	761	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
		Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as

Signaling Pathway.	transduction that regulate cell	described below under
)	proliferation, activation, or	"Hyperproliferative
-	apoptosis are well known in	Disorders"), blood disorders
	the art and may be used or	(e.g., as described below under
	routinely modified to assess	"Immune Activity",
	the ability of polypeptides of	"Cardiovascular Disorders",
	the invention (including	and/or "Blood-Related
	antibodies and agonists or	Disorders"), and infection
	antagonists of the invention) to	(e.g., an infectious disease as
	promote or inhibit immune cell	described below under
	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia.

				the contents of each of which	lymphoma prostate breast
				are herein incomorated by	ling colon pancreatic
				reference in its entirety. T	nuig, coloni, paneleane,
				reference in its entirety.	esopnageal, stomacn, orain,
				cells that may be used	liver, and urinary cancer. Other
				according to these assays are	preferred indications include
•				publicly available (e.g.,	benign dysproliferative
_				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HOFMT75	761	Activation of	Kinase assay. JNK and p38	A highly preferred
			Endothelial Cell	kinase assays for signal	embodiment of the invention
	_		p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
_				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the

invention includes a method for inhibiting endothelial cell growth. A highly preferred	embodiment of the invention includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or
routinely modified to assess the ability of polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) to	promote or inhibit cell	proliferation, activation, and	apoptosis. Exemplary assays for JNK and p38 kinase	activity that may be used or	routinely modified to test JNK	and p38 kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays
																		-								
	-																									

la l	are publicly available (e.g.,	inactivating endothelial cells.
1	through the ATCC).	A highly preferred
<u>田</u>	Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for
<u> </u>	these assays include human	stimulating angiogenisis. An
in	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
19	endothelial cells which line	includes a method for
<u> </u>	venous blood vessels, and are	inhibiting angiogenesis. A
	involved in functions that	highly preferred embodiment
ui.	include, but are not limited to,	of the invention includes a
41	angiogenesis, vascular	method for reducing cardiac
3d	permeability, vascular tone,	hypertrophy. An alternative
al	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy.

intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and

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cavernous), glomus tumors, telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and
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						<u>.</u>																							
		_																	_										

lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,
		-																												

ation of ation of sription gh serum nse element in me cells (such cells).	Activation of transcription through serum response element in immune cells (such as T-cells).

	the invention (including	for stimulating (e.g.,
	antibodies and agonists or	increasing) TNF alpha
	antagonists of the invention) to	production. Preferred
	regulate the serum response	indications include blood
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth. Exemplary assays	Activity", "Blood-Related
	for transcription through the	Disorders", and/or
	SRE that may be used or	"Cardiovascular Disorders"),
	routinely modified to test SRE	Highly preferred indications
	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn's disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
-	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,

	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
	dependent suspension culture	highly preferred indications
	 of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
		leukemia, lymphoma,
		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
-		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
-		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune

reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms and cancers such as, for
	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	762
	HOFNY91

example, leukemia, lymphoma, melanoma, renal cell carcinoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (such as congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve
extravasation. Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit myoblast cell proliferation. Exemplary assays for myoblast cell proliferation that may be used
	Myoblast cell proliferation
	763
	H0F0C73

			
disease, vascular disease, and also as described below under "Cardiovascular Disorders"), stimulating myoblast proliferation, and inhibiting myoblast proliferation.			
or routinely modified to test activity of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) include, for example, assays	disclosed in: Soeta, C., et al. "Possible role for the c-ski gene in the proliferation of myogenic cells in regenerating skeletal muscles of rats" Dev Growth Differ Apr;43(2):155-	64 (2001); Ewton DZ, et al., "IGF binding proteins-4, -5 and -6 may play specialized roles during L6 myoblast proliferation and differentiation" J Endocrinol Mar;144(3):539-53 (1995); and, Pampusch MS, et	al., Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells." J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these

last L6 t t tted frat to form es and ure in			ite cell includes a method for	n, or stimulating endothelial cell	vn in growth. An alternative highly	l or preferred embodiment of the	ssess invention includes a method			or embodiment of the invention	ntion) to includes a method for	stimulating endothelial cell		assays highly preferred embodiment		ed or method for inhibiting	est JNK endothelial cell proliferation.	A highly preferred	of the embodiment of the invention
assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.		Kinase assay. JNK and p38	kinase assays for signal transduction that regulate cell		apoptosis are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	promote or inhibit cell	proliferation, activation, and	apoptosis. Exemplary assays	for JNK and p38 kinase	activity that may be used or	routinely modified to test JNK	and p38 kinase-induced	activity of polypeptides of the
	Caspase (+camptothecin) in SW480	Activation of	p38 or JNK	Signaling Pathway.															
	763	764																	
	НОГОС73	HOGAW62				_													

		invention (including antibodies	includes a method for
		and agonists or antagonists of	stimulating apoptosis of
		the invention) include the	endothelial cells. An
		assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
		Soc Symp 64:29-48 (1999);	A highly preferred
		Chang and Karin, Nature	embodiment of the invention
		410(6824):37-40 (2001); and	includes a method for
		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
		the contents of each of which	alternative highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
		Endothelial cells that may be	inhibiting (e.g., decreasing) the
-		used according to these assays	activation of and/or
		are publicly available (e.g.,	inactivating endothelial cells.
		through the ATCC).	A highly preferred
		Exemplary endothelial cells	embodiment of the invention
		that may be used according to	includes a method for
		these assays include human	stimulating angiogenisis. An
		umbilical vein endothelial cells	alternative highly preferred
	-	(HUVEC), which are	embodiment of the invention
		endothelial cells which line	includes a method for
		venous blood vessels, and are	inhibiting angiogenesis. A
		involved in functions that	highly preferred embodiment
		include, but are not limited to,	of the invention includes a
		angiogenesis, vascular	method for reducing cardiac
		permeability, vascular tone,	hypertrophy. An alternative

and immune cell extravasation.

themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly	preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s	Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,	nemangioendouneilona, angiosarcoma, haemangiopericytoma, lymphangiona, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and

rheumatoid arthritis, cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described
				_																									

n a n.n.a n.n.b de n. b	ation of he preferred embodiment of the invention includes a method for inhibiting (e.g., wn in the production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described involved helow under "Immune helow under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), ot test SRE Highly preferred indications include autoimmune diseases ding customs.
	Assays for the activation of transcription through the Serum Response Element in (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including
	Activation of transcription through serum response element in immune cells (such as T-cells).
-	765
	НОНСН55

Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated	immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly	preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below.	under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other
antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-	368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the	content of each of which are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these	assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies.
gene transcription.	Insulin Secretion
	992
	HOQBJ82

Insulin secretion from	diabetic neuropathy, nerve	
 pancreatic beta cells is	disease and nerve damage	
 upregulated by glucose and	(e.g., due to diabetic	
also by certain	neuropathy), blood vessel	
proteins/peptides, and	blockage, heart disease, stroke,	
disregulation is a key	impotence (e.g., due to diabetic	
component in diabetes.	neuropathy or blood vessel	
Exemplary assays that may be	blockage), seizures, mental	
used or routinely modified to	confusion, drowsiness,	
test for stimulation of insulin	nonketotic hyperglycemic-	
secretion (from pancreatic	hyperosmolar coma,	
cells) by polypeptides of the	cardiovascular disease (e.g.,	
invention (including antibodies	heart disease, atherosclerosis,	
and agonists or antagonists of	microvascular disease,	
the invention) include assays	hypertension, stroke, and other	
disclosed in: Shimizu, H., et	diseases and disorders as	
al., Endocr J, 47(3):261-9	described in the	
(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"	
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,	
17 (1999); Filipsson, K., et al.,	endocrine disorders (as	
 Ann N Y Acad Sci, 865:441-4	described in the "Endocrine	
(1998); Olson, L.K., et al., J	Disorders" section below),	
Biol Chem, 271(28):16544-52	neuropathy, vision impairment	
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and	
Journal of Biomolecular	blindness), ulcers and impaired	
Screening, 4:193-204 (1999),	wound healing, and infection	
 the contents of each of which	(e.g., infectious diseases and	
is herein incorporated by	disorders as described in the	
reference in its entirety.	"Infectious Diseases" section	
Pancreatic cells that may be	below, especially of the	
used according to these assays	urinary tract and skin), carpal	

			are publicly available (e.g.,	tunnel syndrome and
_			through the ATCC) and/or	Dupuytren's contracture).
			may be routinely generated.	An additional highly preferred
			Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
	-		HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
			from Syrian hamster islet cells	weight gain. Additional highly
			transformed with SV40. These	preferred indications are
			cells express glucagon,	complications associated with
			somatostatin, and	insulin resistance.
			glucocorticoid receptors. The	
			cells secrete insulin, which is	
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
			4339-4343, 1981.	
HOSBY40	191	Regulation of	Assays for the regulation of	A highly preferred
		transcription	transcription through the FAS	indication is diabetes mellitus.
. •		through the FAS	promoter element are well-	An additional highly preferred
-		promoter element	known in the art and may be	indication is a complication
		in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
			assess the ability of	diabetic retinopathy, diabetic
			polypeptides of the invention	nephropathy, kidney disease
			(including antibodies and	(e.g., renal failure,

									_							_														
nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic		blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and
agonists or antagonists of the	invention) to activate the FAS	promoter element in a reporter	construct and to regulate	transcription of FAS, a key	enzyme for lipogenesis. FAS	promoter is regulated by many	transcription factors including	SREBP. Insulin increases FAS	gene transcription in livers of	diabetic mice. This	stimulation of transcription is	also somewhat glucose	dependent. Exemplary assays	that may be used or routinely	modified to test for FAS	promoter element activity (in	hepatocytes) by polypeptides	of the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Xiong, S., et al., Proc Natl	Acad Sci U.S.A., 97(8):3948-	53 (2000); Roder, K., et al.,	Eur J Biochem, 260(3):743-51	(1999); Oskouian B, et al.,	Biochem J, 317 (Pt 1):257-65	(1996); Berger, et al., Gene	66:1-10 (1988); and, Cullen,	B., et al., Methods in Enzymol.
								_																	•					

	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,
Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate
	SEAP in HIB/CRE Activation of transcription through NFAT response element in immune cells (such as natural killer cells).
	768
	HOSDJ25 HOSDJ25

NFAT transcription factors and	described below).
 modulate expression of genes	immunodeficiencies (e.g., as
involved in	described below), boosting a T
 immunomodulatory functions.	cell-mediated immune
Exemplary assays for	response, and suppressing a T
transcription through the	cell-mediated immune
NFAT response element that	response. Additional highly
may be used or routinely	preferred indications include
modified to test NFAT-	inflammation and
response element activity of	inflammatory disorders. An
polypeptides of the invention	additional highly preferred
(including antibodies and	indication is infection (e.g., an
agonists or antagonists of the	infectious disease as described
invention) include assays	below under "Infectious
disclosed in Berger et al., Gene	Disease"). Preferred
66:1-10 (1998); Cullen and	indications include neoplastic
Malm, Methods in Enzymol	diseases (e.g., leukemia,
216:362-368 (1992); Henthorn	lymphoma, and/or as described
et al., Proc Natl Acad Sci USA	below under
85:6342-6346 (1988);	"Hyperproliferative
Aramburu et al., J Exp Med	Disorders"). Preferred
182(3):801-810 (1995); De	indications include neoplasms
Boer et al., Int J Biochem Cell	and cancers, such as, for
Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-844 (1999); and	colon, pancreatic, esophageal,
Yeseen et al., J Biol Chem	stomach, brain, liver and
268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents of each of which	indications include benign
are herein incorporated by	dysproliferative disorders and
reference in its entirety. NK	pre-neoplastic conditions, such

			cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HOSDJ25	768	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Apoptosis in pancreatic beta is	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal

associated with induction and	Disorders" section below),
progression of diabetes.	diabetic neuropathy, nerve
Exemplary assays for caspase	disease and nerve damage
apoptosis that may be used or	(e.g., due to diabetic
 routinely modified to test	neuropathy), blood vessel
capase apoptosis activity of	blockage, heart disease, stroke,
polypeptides of the invention	impotence (e.g., due to diabetic
(including antibodies and	neuropathy or blood vessel
 agonists or antagonists of the	blockage), seizures, mental
invention) include the assays	confusion, drowsiness,
disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
(1997); Saini, KS, et al.,	cardiovascular disease (e.g.,
Biochem Mol Biol Int,	heart disease, atherosclerosis,
39(6):1229-36 (1996);	microvascular disease,
Krautheim, A., et al., Br J	hypertension, stroke, and other
Pharmacol, 129(4):687-94	diseases and disorders as
(2000); Chandra J, et al.,	described in the
 Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
 (2001); Suk K, et al., J	section below), dyslipidemia,
 Immunol, 166(7):4481-9	endocrine disorders (as
(2001); Tejedo J, et al., FEBS	described in the "Endocrine
Lett, 459(2):238-43 (1999);	Disorders" section below),
Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
126 (2000); Nor et al., J Vasc	wound healing, and infection
Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
and Karsan and Harlan, J	disorders as described in the
Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
80 (1996); the contents of each	below, especially of the

				of which are herein incorporated by reference in its entirety. Pancreatic cells that	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture).
				may be used according to these	An additional highly preferred
				assays are publicly available (e.g., through the ATCC)	indication is obesity and/or complications associated with
_				and/or may be routinely	obesity. Additional highly
	_			generated. Exemplary	preferred indications include
				pancreatic cells that may be	or alterna
				used according to these assays	weight gain. Aditional
				include RIN-m. RIN-m is a	highly preferred indications are
				rat adherent pancreatic beta	complications associated with
				cell insulinoma cell line	insulin resistance.
				derived from a radiation	
	-			induced transplantable rat islet	
				cell tumor. The cells produce	
				and secrete islet polypeptide	
				hormones, and produce insulin,	
				somatostatin, and possibly	
				glucagon. ATTC: #CRL-2057	
_				Chick et al. Proc. Natl. Acad.	
				Sci. 1977 74:628; AF et al.	
			·	Proc. Natl. Acad. Sci. 1980	
				77:3519.	
	HOSFD58	692	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",

	the ability of polypeptides of	"Cardiovascular Disorders".
	the invention (including	and/or "Blood-Related
	antibodies and agonists or	Disorders"), and infection
	antagonists of the invention) to	(e.g., an infectious disease as
	promote or inhibit immune cell	described below under
	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
	activation, and apoptosis.	preferred indications include
-	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
-	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include

				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neonlastic
				Evenulary money T cells that	discrete and pro-incoplastic
				Exemplary mouse 1 cens man	conditions, such as, for
-				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
		_		line, which is an IL-2	Preferred indications include
		-		dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
		-			transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
-	HPDDC77	1770	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as

	lntomote or inhihit immine cell	described below under
	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
-	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include
	publicly available (e.g.,	benign dysproliferative
	through the ATCC).	disorders and pre-neoplastic
	Exemplary mouse T cells that	conditions, such as, for
	may be used according to these	example, hyperplasia,

metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.			A highly preferred indication is diabetes mellitus. re Additional highly preferred	ray indications include complications associated with diabetes (e.g., diabetic	nephropathy, diabetic nephropathy, kidney disease (e.g., renal failure,	
assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.			Assays for the regulation of transcription through the DMEF1 response element are	well-known in the art and may be used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) to activate the
	IL-2 in Human T cells	Caspase (+paclitaxel) in SW480	Regulation of transcription via DMEF1 response	element in adipocytes and preadipocytes		
	770	770	771			
	HPDDC77	HPDDC77	HPEAD79			

		DAKEEL	oc orapion disorders
		DIMER I response element in a	discases and disolders as
		reporter construct (such as that	described in the "Kenal
		containing the GLUT4	Disorders" section below),
		promoter) and to regulate	diabetic neuropathy, nerve
		insulin production. The	disease and nerve damage
		DMEF1 response element is	(e.g., due to diabetic
		present in the GLUT4	neuropathy), blood vessel
-		promoter and binds to MEF2	blockage, heart disease, stroke,
		transcription factor and another	impotence (e.g., due to diabetic
		transcription factor that is	neuropathy or blood vessel
		required for insulin regulation	blockage), seizures, mental
		of Glut4 expression in skeletal	confusion, drowsiness,
		muscle. GLUT4 is the primary	nonketotic hyperglycemic-
		insulin-responsive glucose	hyperosmolar coma,
		transporter in fat and muscle	cardiovascular disease (e.g.,
		tissue. Exemplary assays that	heart disease, atherosclerosis,
		may be used or routinely	microvascular disease,
		modified to test for DMEF1	hypertension, stroke, and other
		response element activity (in	diseases and disorders as
-		adipocytes and pre-adipocytes)	described in the
		by polypeptides of the	"Cardiovascular Disorders"
		invention (including antibodies	section below), dyslipidemia,
		and agonists or antagonists of	endocrine disorders (as
	-	the invention) include assays	described in the "Endocrine
		disclosed in Thai, M.V., et al., J	Disorders" section below),
		Biol Chem, 273(23):14285-92	neuropathy, vision impairment
		(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
		Chem, 275(21):16323-8	blindness), ulcers and impaired
		(2000); Liu, M.L., et al., J Biol	wound healing, and infection
		Chem, 269(45):28514-21	(e.g., infectious diseases and
		(1994); "Identification of a 30-	disorders as described in the

base pair regulatory element "Infectious Diseases" section and novel DNA binding below, especially of the	•		2000 Aug 4;275(31):23666-73; complications associated with	(1988); and, Cullen, B., et al., preferred indications include	Methods in Enzymol. weight loss or alternatively,	216:362–368 (1992), the weight gain. Additional highly	contents of each of which is preferred indications are	herein incorporated by complications associated with	reference in its entirety. insulin resistance.	Adipocytes and pre-adipocytes	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the mouse 3T3-L1 cell	line which is an adherent	mouse preadipocyte cell line.	Mouse 3T3-L1 cells are a	continuous substrain of 3T3	fibroblasts developed through	clonal isolation. These cells	undergo a pre-adipocyte to	adipose-like conversion under

				culture conditions.	
HP	HPFCL43	772	SEAP in ATP-3T3- L1		
HP	HPFCL43	772	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
_			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
_				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
	•			include assays disclosed in	sclerosis and/or as described
		-		Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated
				85:6342-6346 (1988); and	immune response. Additional

		Diest of of Vinis Conse	highly preferred indications
		Diack et al., vilus Oches	inging proteined marcanons
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		 herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		 assays include the CTLL cell	under "Hyperproliferative
		line, which is an IL-2	Disorders"). Additionally,
	-	dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
		activity.	cancers, such as, for example,
		`	leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
-			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
			anemia, pancytopenia,

leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		n of A highly preferred indication is diabetes mellitus. An lown in additional highly preferred or indication is a complication associated with diabetes (e.g., es of diabetic retinopathy, diabetic nephropathy, kidney disease
		Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	Caspase (+camptothecin) in SW480	Regulation of viability and proliferation of pancreatic beta cells.
	772	773
	HPFCL43	HPIBO15

	antibodies and agonists or	(e.g., renal failure,
	 antagonists of the invention) to	nephropathy and/or other
	regulate viability and	diseases and disorders as
	proliferation of pancreatic beta	described in the "Renal
	cells. For example, the Cell	Disorders" section below),
	Titer-Glo luminescent cell	diabetic neuropathy, nerve
	viability assay measures the	disease and nerve damage
	number of viable cells in	(e.g., due to diabetic
	culture based on quantitation	neuropathy), blood vessel
	of the ATP present which	blockage, heart disease, stroke,
	signals the presence of	impotence (e.g., due to diabetic
	metabolically active cells.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test regulation of viability and	nonketotic hyperglycemic-
	proliferation of pancreatic beta	hyperosmolar coma,
	cells by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Friedrichsen BN,	diseases and disorders as
	et al., Mol Endocrinol,	described in the
	15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
	MA, et al., Endocrinology,	section below), dyslipidemia,
	139(4):1494-9 (1998); Hugl	endocrine disorders (as
	SR, et al., J Biol Chem 1998	described in the "Endocrine
	Jul 10;273(28):17771-9	Disorders" section below),
	(1998), the contents of each of	neuropathy, vision impairment
	which is herein incorporated	(e.g., diabetic retinopathy and
	by reference in its entirety.	blindness), ulcers and impaired
	Pancreatic cells that may be	wound healing, and infection

(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include
used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semiadherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases.
	Production of IL-6
	773
	HPIBO15

blood disorders (e.g., as described below under	will "Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myelome plasmacytome
Assays for immunomodulatory and differentiation factor	proteins produced by a large	variety of cells where the	expression level is strongly	regulated by cytokines, growth	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antihodies and
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				<u> </u>				•	_										_		_								

				organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious
HPIBO15	773	Glucose Production in H4IIE		
HPICB53	774	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
		Apoptosis	caspase apoptosis are well	embodiment of the invention
			known in the art and may be	includes a method for
			used or routinely modified to	stimulating endothelial cell
			assess the ability of	growth. An alternative highly
			polypeptides of the invention	preferred embodiment of the
			(including antibodies and	invention includes a method
			agonists or antagonists of the	for inhibiting endothelial cell
			invention) to promote caspase	growth. A highly preferred
			protease-mediated apoptosis.	embodiment of the invention
			Induction of apoptosis in	includes a method for
			endothelial cells supporting the	stimulating endothelial cell
			vasculature of tumors is	proliferation. An alternative
			associated with tumor	highly preferred embodiment
			regression due to loss of tumor	of the invention includes a
			blood supply. Exemplary	method for inhibiting
			assays for caspase apoptosis	endothelial cell proliferation.
			that may be used or routinely	A highly preferred
			modified to test capase	embodiment of the invention
			apoptosis activity of	includes a method for

leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's
		_											-																	
																														-

			disease and Reynaud"s
			phenomenom, aneurysms,
		_	restenosis; venous and
			lymphatic disorders such as
			thrombophlebitis,
-			lymphangitis, and
	-		lymphedema; and other
			vascular disorders such as
			peripheral vascular disease,
			and cancer. Highly
			preferred indications also
			include trauma such as
			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from
			balloon angioplasty, and
			atheroschlerotic lesions),
			implant fixation, scarring,
			ischemia reperfusion injury,
			rheumatoid arthritis,
		_	cerebrovascular disease, renal
			diseases such as acute renal
			failure, and osteoporosis.
			Additional highly preferred
	_		indications include stroke,
			graft rejection, diabetic or
			other retinopathies, thrombotic
			and coagulative disorders,
			vascularitis, lymph
	_		angiogenesis, sexual disorders,
	_		age-related macular

			/prevention of endometriosis
			and related conditions.
-	-		Additional highly preferred
			indications include fibromas,
			heart disease, cardiac arrest,
	-		heart valve disease, and
			vascular disease.
-			Preferred indications include
			blood disorders (e.g., as
-			described below under
			"Immune Activity", "Blood-
			Related Disorders", and/or
			"Cardiovascular Disorders").
			Preferred indications include
			autoimmune diseases (e.g.,
_			rheumatoid arthritis, systemic
			lupus erythematosis, multiple
			sclerosis and/or as described
			below) and
			immunodeficiencies (e.g., as
			described below). Additional
			preferred indications include
			inflammation and
			inflammatory disorders (such
			as acute and chronic
			inflammatory diseases, e.g.,
			inflammatory bowel disease
			and Crohn's disease), and pain
			management.
HPJBI33 775	Stimulation of	Assays for measuring secretion	A highly preferred

	insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
	from pancreatic	the art and may be used or	An additional highly preferred
	beta cells.	routinely modified to assess	indication is a complication
	-	the ability of polypeptides of	associated with diabetes (e.g.,
		the invention (including	diabetic retinopathy, diabetic
		antibodies and agonists or	nephropathy, kidney disease
		antagonists of the invention) to	(e.g., renal failure,
		stimulate insulin secretion.	nephropathy and/or other
		For example, insulin secretion	diseases and disorders as
		is measured by FMAT using	described in the "Renal
		anti-rat insulin antibodies.	Disorders" section below),
		Insulin secretion from	diabetic neuropathy, nerve
		pancreatic beta cells is	disease and nerve damage
		upregulated by glucose and	(e.g., due to diabetic
		also by certain	neuropathy), blood vessel
		proteins/peptides, and	blockage, heart disease, stroke,
-		disregulation is a key	impotence (e.g., due to diabetic
-		component in diabetes.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (from pancreatic	hyperosmolar coma,
		cells) by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ahren, B., et al.,	diseases and disorders as
		Am J Physiol, 277(4 Pt	described in the
		2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
		al., Endocrinology,	section below), dyslipidemia,
		138(9):3735-40 (1997); Kim,	endocrine disorders (as

			K.H., et al., FEBS Lett.	described in the "Endocrine
			377(2):237 0 (1005): 223	Discussion of continuous
			3//(2).23/-9 (1993); and,	Disorders section below),
			Miraglia S et. al., Journal of	neuropathy, vision impairment
-			Biomolecular Screening,	(e.g., diabetic retinopathy and
			4:193-204 (1999), the contents	blindness), ulcers and impaired
			of each of which is herein	wound healing, and infection
	-		incorporated by reference in its	(e.g., infectious diseases and
			entirety. Pancreatic cells that	disorders as described in the
 -			may be used according to these	"Infectious Diseases" section
			assays are publicly available	below, especially of the
	•		(e.g., through the ATCC)	urinary tract and skin), carpal
			and/or may be routinely	tunnel syndrome and
			generated. Exemplary	Dupuytren's contracture).
_			pancreatic cells that may be	An additional highly preferred
 _			used according to these assays	indication is obesity and/or
			include rat INS-1 cells. INS-1	complications associated with
			cells are a semi-adherent cell	obesity. Additional highly
			line established from cells	preferred indications include
			isolated from an X-ray induced	weight loss or alternatively,
			rat transplantable insulinoma.	weight gain. Aditional
			These cells retain	highly preferred indications are
			characteristics typical of native	complications associated with
			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
_			secretion. References: Asfari	
			et al. Endocrinology 1992	
	,		130:167.	
HPJBI33	775	SEAP in SW480		
HPJBK12	922	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
			of insulin are well-known in	is diabetes mellitus. An
			the art and may be used or	additional highly preferred

routinely modified to assess
the ability of polypeptides of
the invention (including
antibodies and agonists or
antagonists of the invention) to
stimulate insulin secretion.
For example, insulin secretion
is measured by FMAT using
anti-rat insulin antibodies.
Insulin secretion from
pancreatic beta cells is
upregulated by glucose and
also by certain
proteins/peptides, and
disregulation is a key
component in diabetes.
Exemplary assays that may be
used or routinely modified to
test for stimulation of insulin
secretion (from pancreatic
cells) by polypeptides of the
invention (including antibodies
and agonists or antagonists of
the invention) include assays
disclosed in: Shimizu, H., et
al., Endocr J, 47(3):261-9
(2000); Salapatek, A.M., et al.,
Mol Endocrinol, 13(8):1305-
17 (1999); Filipsson, K., et al.,
Ann N Y Acad Sci, 865:441-4
(1998); Olson, L.K., et al., J

		Biol Chem. 271(28):16544-52	neuropathy, vision impairment
		(1996): and, Miraglia S et. al	(e.g., diabetic retinopathy and
		Journal of Biomolecular	blindness), ulcers and impaired
		Screening, 4:193-204 (1999),	wound healing, and infection
		the contents of each of which	(e.g., infectious diseases and
		is herein incorporated by	disorders as described in the
		reference in its entirety.	"Infectious Diseases" section
		Pancreatic cells that may be	below, especially of the
		used according to these assays	urinary tract and skin), carpal
		are publicly available (e.g.,	tunnel syndrome and
		through the ATCC) and/or	Dupuytren's contracture).
		may be routinely generated.	An additional highly preferred
		Exemplary pancreatic cells that	indication is obesity and/or
		may be used according to these	complications associated with
		assays include HITT15 Cells.	obesity. Additional highly
		HITT15 are an adherent	preferred indications include
		epithelial cell line established	weight loss or alternatively,
		from Syrian hamster islet cells	weight gain. Additional highly
		transformed with SV40. These	preferred indications are
-		cells express glucagon,	complications associated with
-		somatostatin, and	insulin resistance.
		glucocorticoid receptors. The	
		cells secrete insulin, which is	
		stimulated by glucose and	
		glucagon and suppressed by	
		somatostatin or	
		glucocorticoids. ATTC# CRL-	
		1777 Refs: Lord and	
		Ashcroft. Biochem. J. 219:	
		547-551; Santerre et al. Proc.	
		Natl. Acad. Sci. USA 78:	

				4339-4343, 1981.	
-	HPJBK12	922	Regulation of	Caspase Apoptosis. Assays for	Preferred embodiments of the
			apoptosis of	caspase apoptosis are well	invention include using
			immune cells (such	known in the art and may be	polypeptides of the invention
			as mast cells).	used or routinely modified to	(or antibodies, agonists, or
				assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
	-			(including antibodies and	prevention, and/or treatment of
-				agonists or antagonists of the	asthma, allergy,
				invention) to regulate caspase	hypersensitivity and
				protease-mediated apoptosis in	inflammation.
				immune cells (such as, for	
				example, in mast cells). Mast	
-	-			cells are found in connective	
	•			and mucosal tissues throughout	
	•			the body, and their activation	
				via immunoglobulin E -	
				antigen, promoted by T helper	
				cell type 2 cytokines, is an	
				important component of	
				allergic disease. Dysregulation	
				of mast cell apoptosis may	
				play a role in allergic disease	
	-			and mast cell tumor survival.	
				Exemplary assays for caspase	
	_			apoptosis that may be used or	
				routinely modified to test	
				capase apoptosis activity	
	-			induced by polypeptides of the	
				invention (including antibodies	
				and agonists or antagonists of	

the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	=	apoptosis are well known in growin. An alternative nigniy the art and may be used or preferred embodiment of the
	HPJBK12 776 Activati Endothe p38 or J Signalir	

for inhibiting endothelial cell growth. A highly preferred embodiment of the invention	includes a method for stimulating endothelial cell	proliferation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.
the ability of polypeptides of the invention (including antibodies and agonists or	antagonists of the invention) to promote or inhibit cell	proliferation, activation, and apoptosis. Exemplary assays	for JNK and p38 kinase activity that may be used or	routinely modified to test JNK	and p38 kinase-induced	activity of polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,
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										_											,			

through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells which line endothelial cells which line venous blood vessels, and are include, but are not limited to, and immune cell extravasation. A highly preferred embodiment of the invention includes a method for reducing cardiac permeability, vascular tone, and immune cell extravasation. A highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. An alternative method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under						
through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation	through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation

hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or	as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular.	endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels	such as diabetes mellitus, as well as diseases of the vessels	arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that	inhibit angiogenesis and/or cardiovascularization. Highly preferred indications	include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s	sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer.	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors.

telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other
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vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as	wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring,	ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred	indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders,	age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and

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	_			vasculai discasc.
				Preferred indications include
_				blood disorders (e.g., as
				described below under
				"Immune Activity", "Blood-
				Related Disorders", and/or
	-			"Cardiovascular Disorders").
				Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HPMDK28	777	Stimulation of	Assays for measuring calcium	A highly preferred
_		Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
		pancreatic beta	and may be used or routinely	An additional highly preferred
		cells.	modified to assess the ability	indication is a complication
			of polypeptides of the	associated with diabetes (e.g.,
			invention (including antibodies	diabetic retinopathy, diabetic
			and agonists or antagonists of	nephropathy, kidney disease
			the invention) to mobilize	(e.g., renal failure,

diseases and disorders as described in the "Renal Disorders" section below)	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,	nonketotic hyperglycemic- hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis,	microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and
calcium. For example, the FLPR assay may be used to measure influx of calcium.	concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause in the control of column to the column t	activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays	that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(10):4589- 601 (1995);Mogami H, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al.,	Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its entirety.

			Pancreatic cells that may be used according to these assays	disorders as described in the "Infections Diseases" section
			are publicly available (e.g.,	below, especially of the
			through the ATCC) and/or	urinary tract and skin), carpal
			may be routinely generated.	tunnel syndrome and
			Exemplary pancreatic cells that	Dupuytren's contracture).
			may be used according to these	An additional highly preferred
 			assays include HITT15 Cells.	indication is obesity and/or
			HITT15 are an adherent	complications associated with
			epithelial cell line established	obesity. Additional highly
			from Syrian hamster islet cells	preferred indications include
			transformed with SV40. These	weight loss or alternatively,
			cells express glucagon,	weight gain. Aditional
			somatostatin, and	highly preferred indications are
			glucocorticoid receptors. The	complications associated with
			cells secrete insulin, which is	insulin resistance.
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78:	
TIME STATE OF THE		,	4339-4343, 1981.	
 HPMDK28	111	SEAP in Jurkat/IL4 promoter (antiCD3		
		co-stim)		
HPMFP40	778	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,

	response element in	(SRE) are well-known in the	reducing) TNF alpha
	immine cells (such	art and may be used or	production. An alternative
	as T-cells).	routinely modified to assess	preferred embodiment of the
	`	the ability of polypeptides of	invention includes a method
		the invention (including	for stimulating (e.g.,
		antibodies and agonists or	increasing) TNF alpha
		antagonists of the invention) to	production. Preferred
		regulate the serum response	indications include blood
		factors and modulate the	disorders (e.g., as described
		expression of genes involved	below under "Immune
		in growth. Exemplary assays	Activity", "Blood-Related
		for transcription through the	Disorders", and/or
		SRE that may be used or	"Cardiovascular Disorders"),
		routinely modified to test SRE	Highly preferred indications
		activity of the polypeptides of	include autoimmune diseases
		the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
		antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
	-	content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly

according to these assays are publicly available (e.g., authority the ATCC). Exemplary mouse T cells that may be used according to these and or as described below assays include the CTLL cell under "Hyperproliferative line, which is an IL-2 bisorders"). Additionally, dependent suspension culture of T cells with cytotoxic activity. Caclis with cytotoxic activity. Every mail ginant glioma, solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative dissorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include benign dysproliferative dissorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include benign dysproliferative dissorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, Hodgkin's disease, acute lymphomas multiple anemia, pancytopenia, hyperparacytomas multiple		
according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma, solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas multiple	myeloma, Burkitt's lymphoma,
	Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	

				disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HPKAL78 779	2	Regulation of transcription via DMEF1 response element in adipocytes and preadipocytes	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The	A highly preferred indication is diabetes mellitus. Additional highly preferred indications include complications associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage

	present in the GLUT4	neuropathy), blood vessel
	promoter and binds to MEF2	blockage, heart disease, stroke,
	 transcription factor and another	impotence (e.g., due to diabetic
	transcription factor that is	neuropathy or blood vessel
	required for insulin regulation	blockage), seizures, mental
	of Glut4 expression in skeletal	confusion, drowsiness,
	muscle. GLUT4 is the primary	nonketotic hyperglycemic-
	insulin-responsive glucose	hyperosmolar coma,
 	transporter in fat and muscle	cardiovascular disease (e.g.,
	tissue. Exemplary assays that	heart disease, atherosclerosis,
	may be used or routinely	microvascular disease,
	modified to test for DMEF1	hypertension, stroke, and other
	response element activity (in	diseases and disorders as
	 adipocytes and pre-adipocytes)	described in the
	by polypeptides of the	"Cardiovascular Disorders"
	invention (including antibodies	section below), dyslipidemia,
	and agonists or antagonists of	endocrine disorders (as
	the invention) include assays	described in the "Endocrine
	disclosed in Thai, M.V., et al., J	Disorders" section below),
	Biol Chem, 273(23):14285-92	neuropathy, vision impairment
-1-	(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
	 Chem, 275(21):16323-8	blindness), ulcers and impaired
	(2000); Liu, M.L., et al., J Biol	wound healing, and infection
	Chem, 269(45):28514-21	(e.g., infectious diseases and
	(1994); "Identification of a 30-	disorders as described in the
 -	base pair regulatory element	"Infectious Diseases" section
	and novel DNA binding	below, especially of the
	 protein that regulates the	urinary tract and skin). An
	human GLUT4 promoter in	additional highly preferred
	transgenic mice", J Biol Chem.	indication is obesity and/or
	2000 Aug 4;275(31):23666-73;	complications associated with

Berger, et al., Grene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.			
	IL-2 in Human T- cell 293T	SEAP in OE-33	VEGF in SW480
	779	779	779
	HPRAL78	HPRAL78	HPRAL78

HPRBC80	780	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the GATA-3	include allergy, asthma, and
		through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
	•		cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
			through the GATA3 response	Preferred indications also
			element are well-known in the	include blood disorders (e.g.,
			art and may be used or	as described below under
			routinely modified to assess	"Immune Activity", "Blood-
			the ability of polypeptides of	Related Disorders", and/or
			the invention (including	"Cardiovascular Disorders").
			antibodies and agonists or	Preferred indications include
			antagonists of the invention) to	autoimmune diseases (e.g.,
			regulate GATA3 transcription	rheumatoid arthritis, systemic
			factors and modulate	lupus erythematosis, multiple
			expression of mast cell genes	sclerosis and/or as described
			important for immune response	below) and
			development. Exemplary	immunodeficiencies (e.g., as
			assays for transcription	described below). Preferred
			through the GATA3 response	indications include neoplastic
			element that may be used or	diseases (e.g., leukemia,
			routinely modified to test	lymphoma, melanoma,
			GATA3-response element	prostate, breast, lung, colon,
			activity of polypeptides of the	pancreatic, esophageal,
			invention (including antibodies	stomach, brain, liver, and
			and agonists or antagonists of	urinary tract cancers and/or as
			the invention) include assays	described below under

disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell Acad Spring Harb Symp Quant Biol 64:563-571 (1999) Rodriguez-Palmene et al., Eur JImmunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and acute lymphocytic anemia Henderson et al., Mol Cell Biol Henderson et al., Mol Cell Biol Rodriguez-Palmene by Referred indications include Rodriguez-Palmene et al., Eur JImmunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and acute lymphocytic anemia Henderson et al., Mol Cell Biol Rodriguez-Palmene by Remplary the ATCC). Exemplary human mast cells house assays include the HMC- Cell Bulkenia, and exhibits Radriguez-Palmene and tissues, hemophilia, hypercoagulation, diabetes meningitis, and Lyme Disease.		Г																					_									
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Flavell et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Bur J Immunol 29(12):3914-3924 (1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell letkemia, and exhibits		Hyperproliterative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, and Lyme Disease.					
			disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-	1 cell line, which is an	immature human mast cell line	established from the peripheral	blood of a patient with mast	cell leukemia, and exhibits	many characteristics of

HP	HPRBC80	780	Activation of	This reporter assay measures	Highly preferred indications
			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
_				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
-				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
			•	agonists or antagonists of the	rheumatoid arthritis, systemic
_				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,
	-			may be used or routinely	prostate, breast, lung, colon,
	-			modified to test NFAT-	pancreatic, esophageal,
				response element activity of	stomach, brain, liver, and
				polypeptides of the invention	urinary tract cancers and/or as
				(including antibodies and	described below under

	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	
	216:362-368 (1992); Henthorn	
	et al., Proc Natl Acad Sci USA	
	85:6342-6346 (1988); De Boer	
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease.
	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
-	Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,
	through the ATCC).	hypercoagulation, diabetes
	Exemplary human mast cells	mellitus, endocarditis,
	that may be used according to	meningitis, and Lyme Disease.
	these assays include the HMC-	•
	1 cell line, which is an	
	immature human mast cell line	
	established from the peripheral	
	blood of a patient with mast	
	cell leukemia, and exhibits	

			many characteristics of	
			immature mast cells.	
 HPRBC80	780	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include blood disorders (e.g.,
		through NFAT	Nuclear Factor of Activated T	as described below under
		response element in	cells (NFAT) response element	"Immune Activity", "Blood-
		immune cells (such	are well-known in the art and	Related Disorders", and/or
		as natural killer	may be used or routinely	"Cardiovascular Disorders").
		cells).	modified to assess the ability	Highly preferred indications
			of polypeptides of the	include autoimmune diseases
			invention (including antibodies	(e.g., rheumatoid arthritis,
			and agonists or antagonists of	systemic lupus erythematosis,
			the invention) to regulate	multiple sclerosis and/or as
			NFAT transcription factors and	described below),
			modulate expression of genes	immunodeficiencies (e.g., as
			involved in	described below), boosting a T
			immunomodulatory functions.	cell-mediated immune
-			Exemplary assays for	response, and suppressing a T
			transcription through the	cell-mediated immune
			NFAT response element that	response. Additional highly
			may be used or routinely	preferred indications include
			modified to test NFAT-	inflammation and
			response element activity of	inflammatory disorders. An
			polypeptides of the invention	additional highly preferred
			(including antibodies and	indication is infection (e.g., an
			agonists or antagonists of the	infectious disease as described
			invention) include assays	below under "Infectious
			disclosed in Berger et al., Gene	Disease"). Preferred
			66:1-10 (1998); Cullen and	indications include neoplastic
			Malm, Methods in Enzymol	diseases (e.g., leukemia,
			216:362-368 (1992); Henthorn	lymphoma, and/or as described

		ms		oma,		al,		rred		pu	nch	e,	ъ.		nia,	nia,	_	<u>۔۔۔</u>		ma,	tons	e e	ۍـ					on,	itis,
a	red	neoplas	is, for	, lymph	t, lung,	esophage	er and	ner prefe	benign	sorders a	ditions,	perplasi	dysplasi	ns also	ncytope	ocytope	acute	ia (ALL)	ultiple	s lymph	ınuloma	ory bow	ıtropeni	asis,	nune	anted		oagulat	ndocard
er liferativ). Prefer	include	s, such	eukemia	te, breas	creatic,	orain, liv	ncer. Oth	include	ative di	stic con	mple, hy	, and/or	ndicatio	emia, pa	, throm	disease,	ic anem	omas, m	Burkitt'	IDS, gra	flammat	psis, neu	ia, psoria	n of imn	o transpl	tissues,	a, hypero	ellitus, e
below under "Hynermroliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,
	D				a	<u> </u>	st			.	Id	as			ıı.							-di	. p	<u>u</u>	ns	re	0	he	<u>d</u>
Sci US	, p Med	5); De	hem Ce	36 (1995	lounum); and	Chem	3 (1993)	of which	ed by	ty. NK		says are	.;		K cells	ording to	he NK-	a huma	with	. <u>2</u>								
et al., Proc Natl Acad Sci USA 85.6342-6346 (1988):	Aramburu et al., J Exp Med	182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used	according to these assays are	publicly available (e.g.,	TCC).	Exemplary human NK cells	that may be used according to	these assays include the NK-	YT cell line, which is a human	natural killer cell line with	cytolytic and cytotoxic								
Proc No. 47-6346	buru et):801-8	et al., In	1(10):1	et al., I	838-84	n et al.,	9):1428	ntents o	rein inc	nce in it	hat may	ding to t	ly avail	through the ATCC).	plary hu	iay be u	assays i	ill line,	ıl killer	rtic and	ķ.							
et al.,	Aram	182(3	Boer 6	Biol 3	Fraser	29(3):	Yesee	268(1	the co	are he	refere	cells t	accord	public	throug	Exem	that m	these	YT ce	natura	cytoly	activity.				•			
												_																	

					meningitis, Lyme Disease, asthma and allergy.
H	HPRBC80	780	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
	**		through serum	Serum Response Element	method for inhibiting (e.g.,
	-		response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
_				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
	_			expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
_				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
_				Malm, Methods in Enzymol	suppressing a T cell-mediated
-	-			216:362-368 (1992); Henthorn	immune response. Additional
	~			et al., Proc Natl Acad Sci USA	highly preferred indications

53(9):3862- inflammatory disorders, and slack et al., treating joint damage in patients with rheumatorid		entirety. 1 Highly preferred indications sed include neoplastic diseases assays are (e.g. lenkemia lymphoma	.g.,	that may be Disorders"). Additionally,	these assays highly preferred indications	iller		melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast, lung, colon, pancreatic.	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	anemia, panevtonenia	lantonania thrombooutonania
85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of which are herein incorporated	oy reference in its entirety. I cells that may be used according to these assays are	publicly available (e.g.,	unougn the AICC). Exemplary T cells that may be	used according to these assays include the NK-YT cell line	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.		_										

					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
_					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
		_			organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
_	HPRBC80	780	Activation of	Assays for the activation of	Preferred indications
			transcription	transcription through the AP1	include neoplastic diseases
	_		through AP1	response element are well-	(e.g., as described below under
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
		-		polypeptides of the invention	"Immune Activity",
				(including antibodies and	"Cardiovascular Disorders",
				agonists or antagonists of the	and/or "Blood-Related
				invention) to modulate growth	Disorders"), and infection
				and other cell functions.	(e.g., an infectious disease as

		Exemplary assays for	described below under
-		transcription through the AP1	"Infectious Disease"). Highly
		response element that may be	preferred indications include
		used or routinely modified to	autoimmune diseases (e.g.,
-		test AP1-response element	rheumatoid arthritis, systemic
		activity of polypeptides of the	lupus erythematosis, multiple
		invention (including antibodies	sclerosis and/or as described
		and agonists or antagonists of	below) and
		the invention) include assays	immunodeficiencies (e.g., as
		disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
	_	et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety.	lung, colon, pancreatic,
		Human T cells that may be	esophageal, stomach, brain,
		used according to these assays	liver, and urinary cancer. Other
		are publicly available (e.g.,	preferred indications include
-		through the ATCC).	benign dysproliferative
		Exemplary human T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the SUPT cell	example, hyperplasia,

		-	line, which is an IL-2 and IL-4 responsive suspension-culture cell line.	metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,
HPRBC80	780	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune

	Evemulary assays for	To suitable but on concentration
	to to the total of the total	response, and suppressing a 1
	ranscription inrougn the	cell-mediated immune
	NFAT response element that	response. Additional highly
	may be used or routinely	preferred indications include
	modified to test NFAT-	inflammation and
	response element activity of	inflammatory disorders. An
	polypeptides of the invention	additional highly preferred
	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988); Serfling	"Hyperproliferative
	et al., Biochim Biophys Acta	Disorders"). Preferred
	1498(1):1-18 (2000); De Boer	indications include neoplasms
	et al., Int J Biochem Cell Biol	and cancers, such as, for
	31(10):1221-1236 (1999);	example, leukemia, lymphoma,
-	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. T	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,
	according to these assays are	metaplasia, and/or dysplasia.
	publicly available (e.g.,	Preferred indications also
	through the ATCC).	include anemia, pancytopenia

			Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HPRBC80	780	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and

		-																										_
immunodeficiencies (e.g., as described below). An	additional highly preferred indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such	as,melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	Tourse the state of the state o
NFKB response element that may be used or rountinely	modified to test NFKB- response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.	
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					Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.
工	HPTTG19	781	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for an alternative highly preferred embodiment of the invention includes a

	ASSA	assays for caspase apoptosis	endothelial cell proliferation	
_	that	that may be used or routinely	A highly preferred	
	ipom	modified to test capase	embodiment of the invention	
	apop	apoptosis activity of	includes a method for	
	polyi	polypeptides of the invention	stimulating apoptosis of	
	(incl	(including antibodies and	endothelial cells. An	
	agon	agonists or antagonists of the	alternative highly preferred	
	inver	invention) include the assays	embodiment of the invention	
-	discle	disclosed in Lee et al., FEBS	includes a method for	
	Lett	Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)	
	Nor 6	Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.	
	209-2	209-218 (2000); and Karsan	A highly preferred	_
	and F	and Harlan, J Atheroscler	embodiment of the invention	
	Thro	Thromb 3(2): 75-80 (1996);	includes a method for	
	the co	the contents of each of which	stimulating angiogenisis. An	
	are h	are herein incorporated by	alternative highly preferred	
	refere	reference in its entirety.	embodiment of the invention	
	Endo	Endothelial cells that may be	includes a method for	
	pesn	used according to these assays	inhibiting angiogenesis. A	
	are p	are publicly available (e.g.,	highly preferred embodiment	
	throu	through commercial sources).	of the invention includes a	
	Exem	Exemplary endothelial cells	method for reducing cardiac	
	that n	that may be used according to	hypertrophy. An alternative	
	these	these assays include bovine	highly preferred embodiment	
	aortic	aortic endothelial cells	of the invention includes a	
	(bAE	(bAEC), which are an example	method for inducing cardiac	
	of en	of endothelial cells which line	hypertrophy. Highly	
	poold	blood vessels and are involved	preferred indications include	
	in fur	in functions that include, but	neoplastic diseases (e.g., as	_
	are no	are not limited to,	described below under	
	angio	angiogenesis, vascular	"Hyperproliferative	

and immune cell extravasation. the cardion (e.g., heart failun a portic sten cardiomyon regurgitatio dysfunctio and athero disease, di intracardia hypertroph infarction, hemodyna as describe "Cardiothelia disorders (disorders (disorders (disorders (disorders (archive) and athero archive) and athero archive cardiothelia disorders (disorders (disorders (archive) archive) archive arteries, candor lympreferred is stimulate a cardiovasse preferred a stimulate a cardiovasse preferred a preferred a stimulate a cardiovasse preferred a preferred a stimulate a cardiovasse preferred a preferred a preferred a stimulate a cardiovasse preferred a preferred a preferred a stimulate a cardiovasse preferred a p		permeability, vascular tone,	Disorders"), and disorders of
(e.g., heart failun aortic stent cardiomyo cardiomyo cardiomyo regungitati dysfunctio and athero disease, di intracardia hypertroph infarction, infarction, infarction, infarction, hemodyna as describe "Cardiova Highly pre include cardiothelia disorderst such as dii well as dii themselve arteries, ca and/or lyn preferred.		and immune cell extravasation.	the cardiovascular system
heart failun aortic sten cardiomyor regurgitati dysfunction and atheror disease, di intracardia hypertroph infarction, hemodyna as describor include control i			(e.g., heart disease, congestive
aortic sten cardiomyo regurgitati dysfunctio and athero disease, di intracardia hypertroph infarction, hemodyna as describe "Cardiova Highly e circlude oc endothelia disorders (disorders (disorders (disorders (and/or lyn preferred . stimulate .			heart failure, hypertension,
cardiomyo regurgitati dysfunctio and athero disease, di intracardia hypertropl infarction, hemodyna as describ "Cardiova Highly pre include ca endothelia disorders (disorders (disorders (disorders (disorders (andor lyn preferred . stimulate . cardiovass			aortic stenosis,
regurgitati dysfunctio and athero disease, di intracardia hypertroph infarction, hemodyna as describos Cardiova Highly pre include cc endothelia disorders t such as dii well as dii whenselve and/or lyn preferred i stimulate cardiovass preferred			cardiomyopathy, valvular
dysfunction and athero disease, di intracardia hypertroph infarction, hemodyna as describe "Cardiova Highly pre include ca endothelia disorders to such as d			regurgitation, left ventricular
and athero disease, di intracardia hypertropt infarction, hemodyna as describe "Cardiova Highly pre include ce endothelia disorders (disorders (disorders (disorders (disorders (disorders (disorders) (disord			dysfunction, atherosclerosis
disease, di intracardia hypertroph infarction, hemodyna as describe "Cardiova Highly pre include cc endothelia disorders t such as dis well as dis themselve arteries, cc and/or lyn preferred i stimulate : cardiovass			and atherosclerotic vascular
intracardia hypertroph infarction, hemodyna as describe "Cardiova Highly pre include condition disorders (disorders to a disorders to a disorder to a di			disease, diabetic nephropathy,
hypertroph infarction, hemodyna as describs "Cardiova Highly pre include ca endothelia disorders (disorders t such as disorders t such as dis well as dis themselve arteries, ca and/or lyn preferred i stimulate : cardiovass			intracardiac shunt, cardiac
infarction, hemodyna as describe "Cardiova Highly pre include ce endothelia disorders (disorders to disorders			hypertrophy, myocardial
hemodyna as describe "Cardiova Highly pre include ce endothelia disorders to disorders to such as disorders to such as disorders to and/or lyn preferred: stimulate a cardiovass preferred: stimulate a cardiovass.			infarction, chronic
as describe "Cardiova" Highly pre include cs endothelia disorders (disorders t such as dis well as dis themselve arteries, cs and/or lyn preferred: stimulate is cardiovass.			hemodynamic overload, and/or
"Cardiova Highly pre include condothelia disorders (disorders) to such as dis well as distremselve arteries, condor lyn preferred is stimulate a cardiovass.			as described below under
Highly pre include ca endothelia disorders to disorders to such as dis well as dis themselve arteries, ca and/or lyn preferred is stimulate is cardiovass.			"Cardiovascular Disorders").
include ca endothelia disorders (disorders taken as disorders disorder	-		Highly preferred indications
endothelia disorders (disorders tisorders) such as disorders tisorders tisorders arteries, cand/or lyn preferred stimulate is cardiovassy preferred.			include cardiovascular,
disorders t disorders t such as dis well as dis themselve arteries, c and/or lyn preferred stimulate i cardiovass			endothelial and/or angiogenic
disorders t such as dis well as dis themselve arteries, c and/or lyn preferred i stimulate i cardiovass			disorders (e.g., systemic
such as dis well as dis themselve arteries, contained and/or lyn preferred stimulate arterious cardiovass			disorders that affect vessels
well as dis themselve arteries, cs and/or lyn preferred stimulate stimulate cardiovass preferred			such as diabetes mellitus, as
themselve arteries, cs and/or lyn preferred stimulate s cardiovass preferred breferred a stimulate a stimulate a cardiovass preferred a preferred a stimulate a st			well as diseases of the vessels
arteries, ca and/or lyn preferred a stimulate a cardiovass.			themselves, such as of the
and/or lyn preferred a stimulate a stimulate a cardiovasa			arteries, capillaries, veins
preferred a stimulate a cardiovasc cardiovasc preferred a preferred a cardiovasc cardiov			and/or lymphatics). Highly
stimulate a cardiovasc cardiovasc preferred a			preferred are indications that
cardiovasc			stimulate angiogenesis and/or
preferred			cardiovascularization. Highly
		•	preferred are indications that
inhibit and			inhibit angiogenesis and/or

cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors,	leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer,	hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,	hemangioendothelioma, angiosarcoma, haemangiopericytoma, Iymphangioma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,
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such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic
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and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic
	-																												
			-																					-					
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					inflammatory bowel disease and Crohn's disease), and pain management.
	HPZAB47	782	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
-				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
				used or routinely modified to	lupus erythematosis, multiple
				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and
				disclosed in Forrer et al., Biol	inflammatory disorders.
				Chem 379(8-9):1101-1110	Highly preferred indications
				(1998); Gupta et al., Exp Cell	also include neoplastic
				Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
				Kyriakis JM, Biochem Soc	lymphoma, and/or as described

				Symp 64:79-48 (1999): Chang	holour under
				ond Voite Metrics	
_				and Narin, Inature	Hyperproliferative
				410(6824):37-40 (2001); and	Disorders"). Highly preferred
				Cobb MH, Prog Biophys Mol	indications include neoplasms
				Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
				the contents of each of which	lymphoma, prostate, breast,
				are herein incorporated by	lung, colon, pancreatic,
				reference in its entirety. T	esophageal, stomach, brain,
				cells that may be used	liver, and urinary cancer. Other
				according to these assays are	preferred indications include
				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
-					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HPZAB47	782	CD152 in Human T		

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11	27.4.2.0	000	Cuis		
<u> </u>	HPZAB47	787	Activation of	Assays for the activation of	Preferred embodiments of the
_			transcription	transcription through the	invention include using
			through NFKB	NFKB response element are	polypeptides of the invention
			response element in	well-known in the art and may	(or antibodies, agonists, or
			neuronal cells (such	be used or routinely modified	antagonists thereof) in
			as SKNMC cells).	to assess the ability of	detection, diagnosis,
		_		polypeptides of the invention	prevention, and/or treatment of
				(including antibodies and	Neurological Diseases and
				agonists or antagonists of the	Disorders (e.g. Alzheimer"s
				invention) to regulate NFKB	Disease, Parkinson"s Disease,
				transcription factors and	Brain Cancer, Seizures).
				modulate expression of	
				neuronal genes. Exemplary	
_				assays for transcription	
				through the NFKB response	
-				element that may be used or	
				routinely modified to test	
				NFKB-response element	
				activity of polypeptides of the	
				invention (including antibodies	
				and agonists or antagonists of	
				the invention) include assays	
				disclosed in: Gill JS, et al.,	
				Neurobiol Dis, 7(4):448-461	
				(2000); Tamatani M, et al., J	
				Biol Chem, 274(13):8531-	
				8538 (1999); Berger et al.,	
				Gene 66:1-10 (1998); Cullen	
				and Malm, Methods in	
				Enzymol 216:362-368 (1992);	

	(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
-	activation, and apoptosis.	preferred indications include
	Exemplary assays for JNK and	autoimmune diseases (e.g.,
	p38 kinase activity that may be	rheumatoid arthritis, systemic
	used or routinely modified to	lupus erythematosis, multiple
	test JNK and p38 kinase-	sclerosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include
	publicly available (e.g.,	benign dysproliferative
	through the ATCC).	disorders and pre-neoplastic
-	Exemplary mouse T cells that	conditions, such as, for
	may be used according to these	example, hyperplasia,
	assays include the CTLL cell	metaplasia, and/or dysplasia.

				line, which is an IL-2	Preferred indications include
_				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt"s lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
-					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HKAABIS	/83	Production of	IFNgamma FMAT. IFNg plays	A highly preferred
			IFNgamma using a	a central role in the immune	embodiment of the invention
			T cells	system and is considered to be	includes a method for
				a proinflammatory cytokine.	stimulating the production of
				IFNg promotes TH1 and	IFNg. An alternative highly
				inhibits TH2 differentiation;	preferred embodiment of the
				promotes IgG2a and inhibits	invention includes a method
				IgE secretion; induces	for inhibiting the production of
				macrophage activation; and	IFNg. Highly preferred
				increases MHC expression.	us
				Assays for immunomodulatory	disorders (e.g., as described
				proteins produced by T cells	below under "Immune
				and NK cells that regulate a	Activity", "Blood-Related
				variety of inflammatory	Disorders", and/or
			-	activities and inhibit TH2	"Cardiovascular Disorders"),
				helper cell functions are well	and infection (e.g., viral

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infections, tuberculosis,	Infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune disease (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiency	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Additional preferred	indications include idiopathic	pulmonary fibrosis. Highly	preferred indications include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred
known in the art and may be	used of fourillery infomitted to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, regulate	inflammatory activities,	modulate TH2 helper cell	function, and/or mediate	humoral or cell-mediated	immunity. Exemplary assays	that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as Interferon	gamma (IFNg), and the	activation of T cells. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160
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	_																													

(2000); G	(2000); Gonzalez et al., J Clin	indications include neoplasms
Lab Anal	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
Billiau et	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
Sci 856:2	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
et al., An	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
15:749-7	15:749-795 (1997), and	esophageal, stomach, brain,
Rheumate	Rheumatology (Oxford)	liver and urinary cancer. Other
38(3):214	38(3):214-20 (1999), the	preferred indications include
contents	contents of each of which are	benign dysproliferative
herein inc	herein incorporated by	disorders and pre-neoplastic
reference	reference in its entirety.	conditions, such as, for
Human T	Human T cells that may be	example, hyperplasia,
used acco	used according to these assays	metaplasia, and/or dysplasia.
may be is	may be isolated using	Preferred indications include
technique	techniques disclosed herein or	anemia, pancytopenia,
otherwise	otherwise known in the art.	leukopenia, thrombocytopenia,
Human T	Human T cells are primary	Hodgkin's disease, acute
human ly	human lymphocytes that	lymphocytic anemia (ALL),
mature in	mature in the thymus and	plasmacytomas, multiple
express a	express a T Cell receptor and	myeloma, Burkitt's lymphoma,
CD3, CD	CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
cells med	cells mediate humoral or cell-	disease, inflammatory bowel
mediated	mediated immunity and may	disease, sepsis, neutropenia,
be preacti	be preactivated to enhance	neutrophilia, psoriasis,
responsiveness to	ness to	suppression of immune
nonnumi	immunomodulatory factors.	reactions to transplanted
	-	organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, Lyme Disease,
		asthma and allergy.

	HRABA80	784	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
				of insulin are well-known in	is diabetes mellitus. An
				the art and may be used or	additional highly preferred
				routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
, -				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Shimizu, H., et	diseases and disorders as
				al., Endocr J, 47(3):261-9	described in the
				(2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
				Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,

		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
		17 (1999); Filipsson, K., et al.,	endocrine disorders (as
		Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
		 (1998); Olson, L.K., et al., J	Disorders" section below),
		 Biol Chem, 271(28):16544-52	neuropathy, vision impairment
		(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
		Journal of Biomolecular	blindness), ulcers and impaired
		Screening, 4:193-204 (1999),	wound healing, and infection
		the contents of each of which	(e.g., infectious diseases and
		 is herein incorporated by	disorders as described in the
		 reference in its entirety.	"Infectious Diseases" section
		 Pancreatic cells that may be	below, especially of the
		 used according to these assays	urinary tract and skin), carpal
		 are publicly available (e.g.,	tunnel syndrome and
		through the ATCC) and/or	Dupuytren's contracture).
		may be routinely generated.	An additional highly preferred
		Exemplary pancreatic cells that	indication is obesity and/or
_	<u></u>	may be used according to these	complications associated with
		assays include HITT15 Cells.	obesity. Additional highly
		HITT15 are an adherent	preferred indications include
	-	epithelial cell line established	weight loss or alternatively,
		from Syrian hamster islet cells	weight gain. Additional highly
		 transformed with SV40. These	preferred indications are
		cells express glucagon,	complications associated with
		somatostatin, and	insulin resistance.
		 glucocorticoid receptors. The	
		cells secrete insulin, which is	
		stimulated by glucose and	
		glucagon and suppressed by	
		somatostatin or	
		glucocorticoids. ATTC# CRL-	
		1777 Refs: Lord and	;

				Ashanot Discham I 210.	
_				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
dH	HDABARO	707	T 11. T	4339-4343, 1981.	
III	ADAOU	104	cells		
HR	HRABA80	784	Activation of	Kinase assay. Kinase assays,	A highly preferred
			Endothelial Cell	for example an Elk-1 kinase	embodiment of the invention
_			ERK Signaling	assay, for ERK signal	includes a method for
			Pathway.	transduction that regulate cell	stimulating endothelial cell
				proliferation or differentiation	growth. An alternative highly
_				are well known in the art and	preferred embodiment of the
_				may be used or routinely	invention includes a method
				modified to assess the ability	for inhibiting endothelial cell
				of polypeptides of the	growth. A highly preferred
				invention (including antibodies	embodiment of the invention
				and agonists or antagonists of	includes a method for
				the invention) to promote or	stimulating endothelial cell
				inhibit cell proliferation,	proliferation. An alternative
-	-			activation, and differentiation.	highly preferred embodiment
				Exemplary assays for ERK	of the invention includes a
				kinase activity that may be	method for inhibiting
				used or routinely modified to	endothelial cell proliferation.
-				test ERK kinase-induced	A highly preferred
				activity of polypeptides of the	embodiment of the invention
**************************************				invention (including antibodies	includes a method for
_				and agonists or antagonists of	stimulating apoptosis of
				the invention) include the	endothelial cells. An
				assays disclosed in Forrer et	alternative highly preferred
				al., Biol Chem 379(8-9):1101-	embodiment of the invention
				1110 (1998); Berra et al.,	includes a method for

	Biochem Pharmacol	inhibiting (e.g., decreasing)
-	(60(8):1171-1178 (2000):	apoptosis of endothelial cells.
	Gupta et al., Exp Cell Res	
	247(2):495-504 (1999); Chang	lang
	and Karin, Nature	includes a method for
	410(6824):37-40 (2001); and	nd stimulating (e.g., increasing)
	Cobb MH, Prog Biophys Mol	
	Biol 71(3-4):479-500 (1999);	9); alternative highly preferred
	the contents of each of which	ich embodiment of the invention
	are herein incorporated by	includes a method for
	reference in its entirety.	inhibiting the activation of
	Endothelial cells that may be	
-	used according to these assays	says inactivating endothelial cells.
	are publicly available (e.g.,	
	through the ATCC).	embodiment of the invention
	Exemplary endothelial cells	ls includes a method for
	that may be used according to	g to stimulating endothelial cell
	these assays include human	n differentiation. An alternative
	umbilical vein endothelial cells	cells highly preferred embodiment
	(HUVEC), which are	of the invention includes a
	endothelial cells which line	e method for inhibiting
	venous blood vessels, and are	are endothelial cell differentiation.
	involved in functions that	A highly preferred
	include, but are not limited to,	to, embodiment of the invention
	angiogenesis, vascular	includes a method for
	permeability, vascular tone,	e, stimulating angiogenisis. An
	and immune cell extravasation.	tion. alternative highly preferred
	-	embodiment of the invention
		includes a method for
		inhibiting angiogenesis.
		A highly preferred

embodiment of the invention	includes a method for reducing	cardiac hypertrophy. An	alternative highly preferred	embodiment of the invention	includes a method for inducing	cardiac hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic
																	-													

disorders that affect vessels such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as
																								-					

prostate, breast, lung, colon, someth, brain, liver, and unimary cancer. Preferred indications include benigm dyspopiliterative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, andror dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease, inflammatory vasculitides, Reynaud's disease, inflammatory wasculitides, Reynaud's phenomenon, aneurysms, restensis, venous and lymphatic disorders such as thrombophebitis, lymphatic disorders such as thrombophebitis, lymphatic disorders such as peripheral vascular disorders and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured listure (e.g., vascular injury such as injury as in the injury such as injury as the as injury and the as injury and an accounter as the as injury and an accounter as the as injury and an accounter as the as injury as the as in																															_
	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and
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				rheumatoid arthritis, systemic
				luming omithemotogic multiple
				lupus erymemanosis, mumpie
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
 -				inflammation and
 ,				inflammatory disorders (such
 				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
			(and Crohn's disease), and pain
				management.
HRACD15	785	Regulation of	Assays for the regulation of	A highly preferred
		transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
		Malic Enzyme in	are well-known in the art and	An additional highly preferred
		hepatocytes	may be used or routinely	indication is a complication
			modified to assess the ability	associated with diabetes (e.g.,
			of polypeptides of the	diabetic retinopathy, diabetic
			invention (including antibodies	nephropathy, kidney disease
			and agonists or antagonists of	(e.g., renal failure,
			the invention) to regulate	nephropathy and/or other
			transcription of Malic Enzyme,	diseases and disorders as
			a key enzyme in lipogenesis.	described in the "Renal
			Malic enzyme is involved in	Disorders" section below),
			lipogenesisand its expression is	diabetic neuropathy, nerve
 -			stimulted by insulin. ME	disease and nerve damage
			promoter contains two direct	(e.g., due to diabetic
 			repeat (DR1)- like elements	neuropathy), blood vessel
			MEp and MEd identified as	blockage, heart disease, stroke,

and DOAD wash	immotonos (a a due to diahetie
	importing (e.g., are to diapetic
 elements. ME promoter may	neuropatny or blood vessel
also responds to AP1 and other	blockage), seizures, mental
 transcription factors.	confusion, drowsiness,
Exemplary assays that may be	nonketotic hyperglycemic-
 used or routinely modified to	hyperosmolar coma,
 test for regulation of	cardiovascular disease (e.g.,
transcription of Malic Enzyme	heart disease, atherosclerosis,
 (in hepatocytes) by	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
 invention) include assays	"Cardiovascular Disorders"
disclosed in: Streeper, R.S., et	section below), dyslipidemia,
 al., Mol Endocrinol,	endocrine disorders (as
12(11):1778-91 (1998);	described in the "Endocrine
Garcia-Jimenez, C., et al., Mol	Disorders" section below),
Endocrinol, 8(10):1361-9	neuropathy, vision impairment
 (1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
Biol Chem, 274(25):17997-	blindness), ulcers and impaired
8004 (1999); Ijpenberg, A., et	wound healing, and infection
al., J Biol Chem,	(e.g., infectious diseases and
 272(32):20108-20117 (1997);	disorders as described in the
 Berger, et al., Gene 66:1-10	"Infectious Diseases" section
(1988); and, Cullen, B., et al.,	below, especially of the
Methods in Enzymol.	urinary tract and skin), carpal
 216:362–368 (1992), the	tunnel syndrome and
contents of each of which is	Dupuytren's contracture).
herein incorporated by	An additional highly preferred
 reference in its entirety.	indication is obesity and/or
Hepatocytes that may be used	complications associated with

			according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays includes the mouse 3T3-L1 cell line. 3T3-L1 is a mouse preadipocyte cell line (adherent). It is a continuous substrain of 3T3 fibroblasts developed through clonal isolation. Cells undergo a preadipocyte to adipose-like conversion under appropriate differentiation culture	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
HRACD15	785	Activation of T-Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation, activation, and apoptosis.	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include

	Exemplan assays for INK and	autoimmine diseases le a
	n38 kinase activity that may be	rheumatoid arthritis systemic
	used or routinely modified to	linis exthematosis multiple
	test MIV and n20 bings	solowood on done of done in the
	test Juny and poo kinase-	scierosis and/or as described
	induced activity of	below) and
	polypeptides of the invention	immunodeficiencies (e.g., as
	(including antibodies and	described below). Additional
	agonists or antagonists of the	highly preferred indications
	invention) include the assays	include inflammation and
	disclosed in Forrer et al., Biol	inflammatory disorders.
	Chem 379(8-9):1101-1110	Highly preferred indications
	(1998); Gupta et al., Exp Cell	also include neoplastic
	Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
	Symp 64:29-48 (1999); Chang	below under
	and Karin, Nature	"Hyperproliferative
	410(6824):37-40 (2001); and	Disorders"). Highly preferred
	Cobb MH, Prog Biophys Mol	indications include neoplasms
	Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
	the contents of each of which	lymphoma, prostate, breast,
	are herein incorporated by	lung, colon, pancreatic,
	reference in its entirety. T	esophageal, stomach, brain,
	cells that may be used	liver, and urinary cancer. Other
	according to these assays are	preferred indications include
	publicly available (e.g.,	benign dysproliferative
	through the ATCC).	disorders and pre-neoplastic
	Exemplary mouse T cells that	conditions, such as, for
,	may be used according to these	example, hyperplasia,
	assays include the CTLL cell	metaplasia, and/or dysplasia.
	line, which is an IL-2	Preferred indications include
	dependent suspension-culture	arthritis, asthma, AIDS,

			cell line with cytotoxic activity.	allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,
HRACD15	785	SEAP in HIB/CRE		mennights, and Lyme Disease.
HRACD15	785	Regulation of	Caspase Apoptosis. Assays for	Preferred embodiments of the
		apoptosis of	caspase apoptosis are well	invention include using
		ımmune cells (such	known in the art and may be	polypeptides of the invention
		as mast cells).	used or routinely modified to	(or antibodies, agonists, or
			assess the ability of	antagonists thereof) in
			polypeptides of the invention	detection, diagnosis,
			(including antibodies and	prevention, and/or treatment of
			agonists or antagonists of the	asthma, allergy,
			invention) to regulate caspase	hypersensitivity and
			protease-mediated apoptosis in	inflammation.
			immune cells (such as, for	
			example, in mast cells). Mast	
			cells are found in connective	
			and mucosal tissues throughout	
			the body, and their activation	
			via immunoglobulin E -	
			antigen, promoted by T helper	

cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 1928):1093-1103 (2000); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are																															
	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are	publicly available (e.g.,
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			through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell	
HRACD15	785	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	THIC.	
HRACJ35	786	Regulation of transcription of Malic Enzyme in hepatocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements ME putative PPAR response elements. ME promoter may	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel
			also responds to Ar I and other transcription factors. Exemplary assays that may be	olockage), serzures, mental confusion, drowsiness, nonketotic hyperglycemic-

rosclerosis,	ease, ke, and other	ders as 'isorders''	slipidemia,	Endocrine below),	ı impairment	nopathy and and and and impaired	d infection	seases and	ibed in the	es" section	kin), carpal	pun	acture).	nly preferred	ty and/or	ociated with	al highly	ons include	matively,	Aditional	ndications are
cardiovascular disease (e.g., heart disease, atherosclerosis,	microvascular disease, hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain.	highly preferred indications are
used or routinely modified to test for regulation of transcription of Malic Enzyme	(in hepatocytes) by polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) include assays	disclosed in: Streeper, R.S., et al., Mol Endocrinol,	12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol	Endocrinol, 8(10):1361-9	(1994); Barroso, I., et al., J Biol Chem. 274(25):17997-	8004 (1999); Ijpenberg, A., et	al., J Biol Chem,	272(32):20108-20117 (1997);	Berger, et al., Gene 66:1-10	(1700), and, Cuncil, D., Ct al., Methods in Enzymol.	216:362–368 (1992), the	contents of each of which is	herein incorporated by	reference in its entirety.	Hepatocytes that may be used	according to these assays are	publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary hepatocytes that
																				-	
																		_			
						-		-		-											

			tone, and immune cell	and cancers such as, for
			extravasation. Exemplary endothelial cells that may be	exampie, ieukemia, iympnoma, melanoma, renal cell
			used according to these assays	carcinoma, and prostate,
			include human umbilical vein	breast, lung, colon, pancreatic,
			endothelial cells (HUVEC),	esophageal, stomach, brain,
			which are available from	liver and urinary cancer. Other
			commercial sources. The	preferred indications include
			expression of VCAM	benign dysproliferative
			(CD106), a membrane-	disorders and pre-neoplastic
			associated protein, can be	conditions, such as, for
		_	upregulated by cytokines or	example, hyperplasia,
			other factors, and contributes	metaplasia, and/or dysplasia.
			to the extravasation of	
			lymphocytes, leucocytes and	
			other immune cells from blood	
			vessels; thus VCAM	
			expression plays a role in	
			promoting immune and	
			inflammatory responses.	
HRACJ35	786	Hexosaminidase in		
		RBL-2H3		
HRDFD27	787	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha

production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders" and/or	"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple	sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative
antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays	SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362- 368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are	publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell

	line, which is an IL-2 dependent suspension culture	Disorders"). Additionally, highly preferred indications
	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
		leukemia, lymphoma,
•		melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,

				hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HRDFD27	787	IL-10 in Human T- cell 2B9		
HRDFD27	787	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention

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stimulating apoptosis of endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An		embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment
and agonists or antagonists of the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.
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methoda profit p	of the invention includes a
hype pref described descri	method for inducing cardiac
pref description of the control of t	hypertrophy. Highly
neop desconding the condition of the con	preferred indications include
"Hy Disk "Hy Disk The I have a mort card and disk disk disk disk disk disk disk dis	neoplastic diseases (e.g., as
"Hy Disc Disc Disc Disc Disc Disc Disc Disc	described below under
Disc the c (e.g. phean aort c ard aort c ard a and a disc and a disc and a ard	"Hyperproliferative
the c.g. (e.g. hear aout card and and and and and and and and and an	Disorders"), and disorders of
(e.g. hear aort card and action of the card and action of the card and and and and and action of the card and and action of the card and action of the card action of	the cardiovascular system
head and and card card dyst and dissembled the card dissembled the	(e.g., heart disease, congestive
aort card card dyst and dise intringingingingingingingingingingingingingi	heart failure, hypertension,
card regulation of the control of th	aortic stenosis,
regregative dyst and dise intra hyp infa as d as d "Ca Hig incl incl incl incl incl incl incl incl	cardiomyopathy, valvular
dyst and dise intra intr	regurgitation, left ventricular
and dise intra hyp hyp infa as d as d as d "Ca Hig incl incl incl incl incl incl incl incl	dysfunction, atherosclerosis
dise intra hyp infa infa as d as	and atherosclerotic vascular
intra hyp infa hem hem as d as d "Ca "Ca Hig lincl incl end end disc disc disc	disease, diabetic nephropathy,
hypinfa infa infa infa infa as d "Ca "Ca "incl incl incl incl incl incl incl incl	intracardiac shunt, cardiac
infa herr as d as d "Ca Hig incl end disc disc	hypertrophy, myocardial
as d "Ca "Hig Hig incl end end disc disc	infarction, chronic
as d "Ca Hig incl end end disc	hemodynamic overload, and/or
"Ca High High High High High High High High	as described below under
Hig incl incl end end disc disc disc disc	"Cardiovascular Disorders").
incl end disc disc	Highly preferred indications
end disc	include cardiovascular,
disc disc	endothelial and/or angiogenic
disc	disorders (e.g., systemic
	disorders that affect vessels
	such as diabetes mellitus, as
wel	well as diseases of the vessels
ther	themselves, such as of the

arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or	cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity	to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (canillary and	cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred

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ign	rs and	pre-neoplastic conditions, such	lasia,	lasia.	tions	ease,		hypertension, coronary artery				JS,		h as				as	ase,		Q		red	ary	from		٠,	ည်	ury.
indications include benign	dysproliferative disorders and	ndition	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	ronary	atory	vasculitides, Reynaud"s	and"s	phenomenom, aneurysms,	s and	lymphatic disorders such as	•	-	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	lighly	preferred indications also	ich as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,
s inclu	rative	istic co	mple,	ı, and/c	ferred	le arteı	herosc	on, co	disease, inflammatory	s, Rey	disease and Reynaud's	om, an	restenosis; venous and	disord	thrombophlebitis,	lymphangitis, and	na; anc	sorder	vascul	and cancer. Highly	ndicati	include trauma such as	urns, aı	, vascu	jury re	gioplas	erotic l	ation,	sperfus
cation	prolife	neopla	for exa	aplasia	hly pre	incluc	n as, at	ertensi	ase, in	ulitide	ase an	nomen	enosis;	phatic	mbopk	phangi	pheder	ular di	pheral	cancer	erred ii	ude tra	nds, bu	le (e.g.	ı as, inj	on an	roschle	ant fix	emia re
indi	dys	- bre-	as,	met	Hig	also	snc	hyp	dise	vas	dise	bhe	rest	lym	thro	lym	lym	vasc	peri	and	pref	incl	mom	tissc	such	balle	athe	jmp	isch
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		cere	cerebrovascular disease, renal
		dise	diseases such as acute renal
		failu	failure, and osteoporosis.
		PPA	Additional highly preferred
		ipui	indications include stroke,
		graf	graft rejection, diabetic or
		othe	other retinopathies, thrombotic
		and	and coagulative disorders,
		vasc	vascularitis, lymph
		angi	angiogenesis, sexual disorders,
		age	age-related macular
		gap	degeneration, and treatment
		/pre	/prevention of endometriosis
		and	and related conditions.
		Add	Additional highly preferred
		indic	indications include fibromas,
	-	hear	heart disease, cardiac arrest,
		hear	heart valve disease, and
		vasc	vascular disease.
		Pref	Preferred indications include
		bloo	blood disorders (e.g., as
		desc	described below under
_		"Imi	"Immune Activity", "Blood-
		Rela	Related Disorders", and/or
		"Car	"Cardiovascular Disorders").
		Pref	Preferred indications include
		auto	autoimmune diseases (e.g.,
		rhen	rheumatoid arthritis, systemic
		ndnI	lupus erythematosis, multiple
	-	scler	sclerosis and/or as described
			helow) and

				immunodeficiencies (e.g., as
				described below). Additional
				preferred indications include
				inflammation and
_				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HRDFD27	787	Activation of	Assays for the activation of	Highly preferred indications
		transcription	transcription through the	include inflammation and
		through NFKB	NFKB response element are	inflammatory disorders.
		response element in	well-known in the art and may	Highly preferred indications
		immune cells (such	be used or routinely modified	include blood disorders (e.g.,
		as natural killer	to assess the ability of	as described below under
		cells).	polypeptides of the invention	"Immune Activity", "Blood-
			(including antibodies and	Related Disorders", and/or
			agonists or antagonists of the	"Cardiovascular Disorders").
			invention) to regulate NFKB	Highly preferred indications
			transcription factors and	include autoimmune diseases
			modulate expression of	(e.g., rheumatoid arthritis,
			immunomodulatory genes.	systemic lupus erythematosis,
			Exemplary assays for	multiple sclerosis and/or as
			transcription through the	described below), and
			NFKB response element that	immunodeficiencies (e.g., as
			may be used or rountinely	described below). An
			modified to test NFKB-	additional highly preferred
			response element activity of	indication is infection (e.g.,
			polypeptides of the invention	AIDS, and/or an infectious
			(including antibodies and	disease as described below

	agonists or antagonists of the	under "Infectious Disease")
-	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Valle	Disorders"). Highly preferred
	Blazquez et al, Immunology	indications include neoplasms
	90(3):455-460 (1997);	and cancers, such as, for
	Aramburau et al., J Exp Med	example, melanoma, renal cell
	82(3):801-810 (1995); and	carcinoma, leukemia,
	Fraser et al., 29(3):838-844	lymphoma, and prostate,
	(1999), the contents of each of	breast, lung, colon, pancreatic,
	which are herein incorporated	esophageal, stomach, brain,
	by reference in its entirety.	liver and urinary cancer. Other
	NK cells that may be used	preferred indications include
	according to these assays are	benign dysproliferative
-	publicly available (e.g.,	disorders and pre-neoplastic
	through the ATCC).	conditions, such as, for
	Exemplary human NK cells	example, hyperplasia,
	that may be used according to	metaplasia, and/or dysplasia.
	these assays include the NKL	Preferred indications also
	cell line, which is a human	include anemia, pancytopenia,
	natural killer cell line	leukopenia, thrombocytopenia,
	established from the peripheral	Hodgkin's disease, acute
	blood of a patient with large	lymphocytic anemia (ALL),
	granular lymphocytic	plasmacytomas, multiple
	leukemia. This IL-2 dependent	myeloma, Burkitt's lymphoma,
	suspension culture cell line has	arthritis, AIDS, granulomatous
	a morphology resembling that	disease, inflammatory bowel

				of activated NK cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
		-			hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HRGBL78	788	Stimulation of	Assays for measuring secretion	A highly preferred
			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
=		_		antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
	÷			anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
			,	upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
			-	component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
	-			test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,

cells) by polyneptides of the	cardiovascular disease (e.g.,
invention (including antibodies	
 and agonists or antagonists of	
the invention) include assays	hypertension, stroke, and other
 disclosed in: Ahren, B., et al.,	diseases and disorders as
Am J Physiol, 277(4 Pt	described in the
2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
 al., Endocrinology,	section below), dyslipidemia,
138(9):3735-40 (1997); Kim,	endocrine disorders (as
K.H., et al., FEBS Lett,	described in the "Endocrine
377(2):237-9 (1995); and,	Disorders" section below),
Miraglia S et. al., Journal of	neuropathy, vision impairment
 Biomolecular Screening,	(e.g., diabetic retinopathy and
4:193-204 (1999), the contents	blindness), ulcers and impaired
of each of which is herein	wound healing, and infection
 incorporated by reference in its	(e.g., infectious diseases and
 entirety. Pancreatic cells that	disorders as described in the
 may be used according to these	"Infectious Diseases" section
assays are publicly available	below, especially of the
(e.g., through the ATCC)	urinary tract and skin), carpal
and/or may be routinely	tunnel syndrome and
generated. Exemplary	Dupuytren's contracture).
 pancreatic cells that may be	An additional highly preferred
used according to these assays	indication is obesity and/or
include rat INS-1 cells. INS-1	complications associated with
cells are a semi-adherent cell	obesity. Additional highly
 line established from cells	preferred indications include
isolated from an X-ray induced	weight loss or alternatively,
rat transplantable insulinoma.	weight gain. Aditional
 These cells retain	highly preferred indications are
characteristics typical of native	complications associated with

			pancreatic beta cells including	insulin resistance.
			glucose inducible insulin	
			secretion. References: Astari	
			et al. Endocrinology 1992 130:167.	
HROAJ03	789	IL-4 in HMC		
HROAJ03	789	Activation of	Kinase assay. JNK and p38	A highly preferred
		Endothelial Cell	kinase assays for signal	embodiment of the invention
		p38 or JNK	transduction that regulate cell	includes a method for
		Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
	-		apoptosis are well known in	growth. An alternative highly
			the art and may be used or	preferred embodiment of the
			routinely modified to assess	invention includes a method
			the ability of polypeptides of	for inhibiting endothelial cell
_			the invention (including	growth. A highly preferred
			antibodies and agonists or	embodiment of the invention
			antagonists of the invention) to	includes a method for
			promote or inhibit cell	stimulating endothelial cell
			proliferation, activation, and	proliferation. An alternative
			apoptosis. Exemplary assays	highly preferred embodiment
			for JNK and p38 kinase	of the invention includes a
	_		activity that may be used or	method for inhibiting
			routinely modified to test JNK	endothelial cell proliferation.
			and p38 kinase-induced	A highly preferred
			activity of polypeptides of the	embodiment of the invention
			invention (including antibodies	includes a method for
			and agonists or antagonists of	stimulating apoptosis of
			the invention) include the	endothelial cells. An
			assays disclosed in Forrer et	alternative highly preferred
-			al., Biol Chem 379(8-9):1101-	embodiment of the invention
			1110 (1998); Gupta et al., Exp	includes a method for

	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
-	 Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	 Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
-	 the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
_	reference in its entirety.	includes a method for
	 Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	 are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	 Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for
	these assays include human	stimulating angiogenisis. An
	 umbilical vein endothelial cells	alternative highly preferred
	 (HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
	 venous blood vessels, and are	inhibiting angiogenesis. A
	involved in functions that	highly preferred embodiment
	include, but are not limited to,	of the invention includes a
	 angiogenesis, vascular	method for reducing cardiac
	permeability, vascular tone,	hypertrophy. An alternative
	 and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as

_																		_												
described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly
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				preferred are indications that	c that
-				protein are marcanon	mun ci
				inhibit angiogenesis and/or	d/or
_	_		_	cardiovascularization.	
				Highly preferred indications	tions
				include antiangiogenic activity	activity
		_	-	to treat solid tumors,	
				leukemias, and Kaposi"s	s
			•	sarcoma, and retinal disorders.	sorders.
				Highly preferred indications	tions
				include neoplasms and cancer,	cancer,
				such as, Kaposi"s sarcoma,	ma,
				hemangioma (capillary and	and
			-	cavernous), glomus tumors,	nors,
				telangiectasia, bacillary	
		~		angiomatosis,	
				hemangioendothelioma,	
				angiosarcoma,	
	_			haemangiopericytoma,	
			. .	lymphangioma,	
				lymphangiosarcoma. Highly	lighly
		-	,	preferred indications also	os
				include cancers such as,	
				prostate, breast, lung, colon,	olon,
				pancreatic, esophageal,	-
				stomach, brain, liver, and	pu
		_		urinary cancer. Preferred	- -
				indications include benign	ign
				dysproliferative disorders and	ers and
				pre-neoplastic conditions, such	ns, such
				as, for example, hyperplasia,	lasia,
				metaplasia, and/or dysplasia.	lasia.

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Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke.
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graft rejection, diabetic or
other retinopathies, thrombotic
and coagulative disorders,
 vascularitis, lymph
angiogenesis, sexual disorders,
age-related macular
degeneration, and treatment
/prevention of endometriosis
and related conditions.
 Additional highly preferred
indications include fibromas,
 heart disease, cardiac arrest,
 heart valve disease, and
vascular disease.
 Preferred indications include
blood disorders (e.g., as
 described below under
"Immune Activity", "Blood-
 Related Disorders", and/or
 "Cardiovascular Disorders").
 Preferred indications include
autoimmune diseases (e.g.,
rheumatoid arthritis, systemic
lupus erythematosis, multiple
sclerosis and/or as described
below) and
immunodeficiencies (e.g., as
described below). Additional
preferred indications include
inflammation and
inflammatory disorders (such

					as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
	HROAJ39	790	Stimulation of Calcium Flux in pancreatic beta	Assays for measuring calcium flux are well-known in the art and may be used or routinely	A highly preferred indication is diabetes mellitus. An additional highly preferred
			cells.	modified to assess the ability of polypeptides of the invention (including antibodies	indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic
				and agonists or antagonists of the invention) to mobilize	nephropathy, kidney disease (e.g., renal failure,
				calcium. For example, the FLPR assay may be used to	nephropathy and/or other diseases and disorders as
				measure influx of calcium.	described in the "Renal
				concentrations of cytosolic	diabetic neuropathy, nerve
_				calcium compared to much higher extracellular calcium.	disease and nerve damage (e.g., due to diabetic
				Extracellular factors can cause	neuropathy), blood vessel
				an influx of calcium, leading to	blockage, heart disease, stroke, importance (e.g., due to diabetic.)
_				responsive signaling pathways	neuropathy or blood vessel
				and alterations in cell	blockage), seizures, mental
				tunctions. Exemplary assays that may be used or routinely	contusion, drowsiness,
				modified to measure calcium	hyperosmolar coma,
				flux by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,

			somatostatin or glucocorticoids. ATTC# CRL- 1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc.	
			Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
HROBD68	791	Regulation of	Caspase Apoptosis. Assays	A highly preferred
		apoptosis in	for caspase apoptosis are well	indication is diabetes mellitus.
		pancreatic beta	known in the art and may be	An additional highly preferred
		cells.	used or routinely modified to	indication is a complication
			assess the ability of	associated with diabetes (e.g.,
			polypeptides of the invention	diabetic retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to promote caspase	nephropathy and/or other
			protease-mediated apoptosis.	diseases and disorders as
			Apoptosis in pancreatic beta is	described in the "Renal
			associated with induction and	Disorders" section below),
			progression of diabetes.	diabetic neuropathy, nerve
			Exemplary assays for caspase	disease and nerve damage
			apoptosis that may be used or	(e.g., due to diabetic
			routinely modified to test	neuropathy), blood vessel
			capase apoptosis activity of	blockage, heart disease, stroke,
			polypeptides of the invention	impotence (e.g., due to diabetic
			(including antibodies and	neuropathy or blood vessel
			agonists or antagonists of the	blockage), seizures, mental
			invention) include the assays	confusion, drowsiness,
			disclosed in: Loweth, AC, et	nonketotic hyperglycemic-
			al., FEBS Lett, 400(3):285-8	hyperosmolar coma,
			(1997); Saini, KS, et al.,	cardiovascular disease (e.g.,

	B	Biochem Mol Biol Int.	heart disease, atherosclerosis.
	<u>~</u>	39(6):1229-36 (1996):	microvascular disease.
	X	Krautheim. A., et al., Br J	hypertension, stroke, and other
	<u>a</u>	Pharmacol, 129(4):687-94	diseases and disorders as
		(2000); Chandra J, et al.,	described in the
	Ω	Diabetes, 50 Suppl 1:S44-7	"Cardiovascular Disorders"
		(2001); Suk K, et al., J	section below), dyslipidemia,
	II —	Immunol, 166(7):4481-9	endocrine disorders (as
		(2001); Tejedo J, et al., FEBS	described in the "Endocrine
		Lett, 459(2):238-43 (1999);	Disorders" section below),
	Z	Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
	4	455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
	al	al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
		126 (2000); Nor et al., J Vasc	wound healing, and infection
		Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
	<u>an</u>	and Karsan and Harlan, J	disorders as described in the
	<u> </u>	Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
-	8	80 (1996); the contents of each	below, especially of the
	0	of which are herein	urinary tract and skin), carpal
	ni	incorporated by reference in its	tunnel syndrome and
	ia ei	entirety. Pancreatic cells that	Dupuytren's contracture).
		may be used according to these	An additional highly preferred
-	as	assays are publicly available	indication is obesity and/or
	a)	(e.g., through the ATCC)	complications associated with
	aı	and/or may be routinely	obesity. Additional highly
	50	generated. Exemplary	preferred indications include
	ğ	pancreatic cells that may be	weight loss or alternatively,
	sn _	used according to these assays	weight gain. Aditional
	ui _	include RIN-m. RIN-m is a	highly preferred indications are
	ra	rat adherent pancreatic beta	complications associated with
	93	cell insulinoma cell line	insulin resistance.

			induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980	
HSATR82	792	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,

antagonists of the invention)	Crohn"s disease, multiple
 include assays disclosed in	sclerosis and/or as described
 Berger et al., Gene 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	boosting a T cell-mediated
 368 (1992); Henthorn et al.,	immune response, and
Proc Natl Acad Sci USA	suppressing a T cell-mediated
 85:6342-6346 (1988); and	immune response. Additional
Black et al., Virus Genes	highly preferred indications
 12(2):105-117 (1997), the	include inflammation and
content of each of which are	inflammatory disorders, and
herein incorporated by	treating joint damage in
 reference in its entirety. T	patients with rheumatoid
 cells that may be used	arthritis. An additional highly
 according to these assays are	preferred indication is sepsis.
publicly available (e.g.,	Highly preferred indications
through the ATCC).	include neoplastic diseases
Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
may be used according to these	and/or as described below
 assays include the CTLL cell	under "Hyperproliferative
 line, which is an IL-2	Disorders"). Additionally,
dependent suspension culture	highly preferred indications
 of T cells with cytotoxic	include neoplasms and
activity.	cancers, such as, for example,
	leukemia, lymphoma,
_	melanoma, glioma (e.g.,
	malignant glioma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other

Activation of T-	793 Activation of T-

	Signaling Pathway.	transduction that regulate cell	described below under
)	proliferation, activation, or	"Hyperproliferative
		apoptosis are well known in	Disorders"), blood disorders
		the art and may be used or	(e.g., as described below under
		routinely modified to assess	"Immune Activity",
		the ability of polypeptides of	"Cardiovascular Disorders",
		the invention (including	and/or "Blood-Related
		antibodies and agonists or	Disorders"), and infection
		antagonists of the invention) to	(e.g., an infectious disease as
		promote or inhibit immune cell	described below under
		(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
		activation, and apoptosis.	preferred indications include
		Exemplary assays for JNK and	autoimmune diseases (e.g.,
		p38 kinase activity that may be	rheumatoid arthritis, systemic
		used or routinely modified to	lupus erythematosis, multiple
		test JNK and p38 kinase-	sclerosis and/or as described
		induced activity of	below) and
		polypeptides of the invention	immunodeficiencies (e.g., as
		(including antibodies and	described below). Additional
		agonists or antagonists of the	highly preferred indications
-		invention) include the assays	include inflammation and
		disclosed in Forrer et al., Biol	inflammatory disorders.
		Chem 379(8-9):1101-1110	Highly preferred indications
		(1998); Gupta et al., Exp Cell	also include neoplastic
		Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
		Kyriakis JM, Biochem Soc	lymphoma, and/or as described
		Symp 64:29-48 (1999); Chang	below under
-		and Karin, Nature	"Hyperproliferative
		410(6824):37-40 (2001); and	Disorders"). Highly preferred
		Cobb MH, Prog Biophys Mol	indications include neoplasms
		Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,

			the contents of each of which	lymphoma, prostate, breast,
			are nerein incorporated by reference in its entirety. T	lung, colon, pancreatic, esonhageal, stomach brain
			cells that may be used	liver, and urinary cancer. Other
			according to these assays are	preferred indications include
			publicly available (e.g.,	benign dysproliferative
			through the ATCC).	disorders and pre-neoplastic
			Exemplary mouse T cells that	conditions, such as, for
			may be used according to these	example, hyperplasia,
			assays include the CTLL cell	metaplasia, and/or dysplasia.
			line, which is an IL-2	Preferred indications include
			dependent suspension-culture	arthritis, asthma, AIDS,
			cell line with cytotoxic	allergy, anemia, pancytopenia,
			activity.	leukopenia, thrombocytopenia,
				Hodgkin"s disease, acute
		-		lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt"s lymphoma,
				granulomatous disease,
				inflammatory bowel disease,
	_			sepsis, psoriasis, suppression
				of immune reactions to
				transplanted organs and
				tissues, endocarditis,
37H/1 V 3H	702	TO ANG NI		meningitis, and Lyme Disease.
COLI	193	ICAM in Normal		
		Fritheliae		
HSAVH65	793	II8 in Normal		
		Human Bronchial		
		Epitheliae		

transcription via
DMEF1 response
element in
adipocytes and pre-
adipocytes

invention (including antibodies	section below), dyslipidemia,
 and agonists or antagonists of	endocrine disorders (as
the invention) include assays	described in the "Endocrine
 disclosed in Thai, M.V., et al., J	Disorders" section below),
 Biol Chem, 273(23):14285-92	neuropathy, vision impairment
(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
 Chem, 275(21):16323-8	blindness), ulcers and impaired
(2000); Liu, M.L., et al., J Biol	wound healing, and infection
 Chem, 269(45):28514-21	(e.g., infectious diseases and
(1994); "Identification of a 30-	disorders as described in the
 base pair regulatory element	"Infectious Diseases" section
 and novel DNA binding	below, especially of the
 protein that regulates the	urinary tract and skin). An
 human GLUT4 promoter in	additional highly preferred
 transgenic mice", J Biol Chem.	indication is obesity and/or
 2000 Aug 4;275(31):23666-73;	complications associated with
Berger, et al., Gene 66:1-10	obesity. Additional highly
(1988); and, Cullen, B., et al.,	preferred indications include
Methods in Enzymol.	weight loss or alternatively,
216:362–368 (1992), the	weight gain. Additional highly
 contents of each of which is	preferred indications are
 herein incorporated by	complications associated with
 reference in its entirety.	insulin resistance.
Adipocytes and pre-adipocytes	
 that may be used according to	
 these assays are publicly	
available (e.g., through the	
 ATCC) and/or may be	
routinely generated.	
Exemplary cells that may be	
used according to these assays	

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below) and	imminodeficiencies (e.g., as	described helow) Preferred	indications include neonlestic	indications include heopiasuc	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune
modulate expression of genes	involved in	imminomodulatory functions	The state of the s	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-	16338 (1995), and Turner et	al., J Exp Med 188:527-537	(1998), the contents of each of	which are herein incorporated	by reference in its entirety.	Mast cells that may be used
				•	•														-												
																	-				•										

reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	
according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	794
	HSAWD74

HSAWZ41 HSAWZ41	viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	Activation of transcription of transcr
HSAWZ41 HSAWZ41		795
		HSAWZ41 HSAWZ41

nephropathy and/or other diseases and disorders as described in the "Renal Disorders"	Disorders" section below), diabetic neuropathy, nerve disease and nerve damage	(e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental confusion, drowsiness.	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"		endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and
functions. For example, a 3T3-L1/CRE reporter assay may be used to identify factors	that activate the cAMP signaling pathway. CREB plays a major role in	adipogenesis, and is involved in differentiation into	adipocytes. CRE contains the binding sequence for the	transcription factor CREB	(CRE binding protein). Exemplary assays for	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Reusch	et al., Mol Cell Biol	20(3):1008-1020 (2000); and	Klemm et al J Biol Chem

		273:917-923 (1998), the contents of each of which are	disorders as described in the
		herein incorporated by	below, especially of the
		reference in its entirety. Pre-	urinary tract and skin), carpal
		adipocytes that may be used	tunnel syndrome and
		according to these assays are	Dupuytren's contracture).
		publicly available (e.g.,	Additional highly preferred
_		through the ATCC) and/or	indications are complications
		may be routinely generated.	associated with insulin
		Exemplary mouse adipocyte	resistance.
		cells that may be used	
-		according to these assays	
		include 3T3-L1 cells. 3T3-L1	
		is an adherent mouse	
		preadipocyte cell line that is a	
_		continuous substrain of 3T3	
		fibroblast cells developed	
_		through clonal isolation and	
		undergo a pre-adipocyte to	
-		adipose-like conversion under	
		appropriate differentiation	
		conditions known in the art.	
HSAWZ41 795	Activation of	Assays for the activation of	Preferred indications
	transcription	transcription through the AP1	include neoplastic diseases
	through AP1	response element are known in	(e.g., as described below under
	response element in	the art and may be used or	"Hyperproliferative
	immune cells (such	routinely modified to assess	Disorders"), blood disorders
	as T-cells).	the ability of polypeptides of	(e.g., as described below under
		the invention (including	"Immune Activity",
		antibodies and agonists or	"Cardiovascular Disorders",
		antagonists of the invention) to	and/or "Blood-Related

										_																				
Disorders"), and infection		described below under	winfectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and nre-neonlastic
modulate growth and other cell	functions. Exemplary assays	for transcription through the	AP1 response element that	may be used or routinely	modified to test AP1-response	element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1988); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Rellahan et al., J Biol Chem	272(49):30806-30811 (1997);	Chang et al., Mol Cell Biol	18(9):4986-4993 (1998); and	Fraser et al., Eur J Immunol	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that
			-								•															-				

				may be used according to these	conditions, such as, for
				assays include the CTLL cell	example, hyperplasia,
			-	line, which is an IL-2	metaplasia, and/or dysplasia.
				dependent suspension-culture	Preferred indications include
				cell line with cytotoxic	arthritis, asthma, AIDS,
				activity.	allergy, anemia, pancytopenia,
-					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
_					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HSAWZ41	795	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include asthma, allergy,
			through NFKB	NFKB response element are	hypersensitivity reactions, and
			response element in	well-known in the art and may	inflammation. Preferred
			immune cells (such	be used or routinely modified	indications include infection
			as EOL1 cells).	to assess the ability of	(e.g., an infectious disease as
				polypeptides of the invention	described below under
				(including antibodies and	"Infectious Disease"),
				agonists or antagonists of the	immunological disorders,
				invention) to regulate NFKB	inflammation and
				transcription factors and	inflammatory disorders (e.g.,
	_	_	770	modulate expression of	as described below under
				immunomodulatory genes.	"Immune Activity", and

					_																				
"Blood-Related Disorders"). Preferred indications include	autoniniume diseases (e.g., rheumatoid arthritis, systemic luous ervthematosis, multiple	sclerosis and/or as described below) and	immunodeficiencies (e.g., as	described below).																					
Exemplary assays for transcription through the	may be used or rountinely modified to test NFKB-	response element activity of polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	For example, a reporter assay	(which measures increases in	transcription inducible from a	NFkB responsive element in	EOL-1 cells) may link the	NFKB element to a repeorter	gene and binds to the NFKB
												-													-
				_					_																

	antihodies and agonists or	Dreferred indications include	_
	anticource and agomets of	intrinca marcanoms merace	
`	antagonists of the invention) to	autoimmune diseases (e.g.,	
	regulate GATA3 transcription	rheumatoid arthritis, systemic	
	factors and modulate	lupus erythematosis, multiple	
	expression of mast cell genes	sclerosis and/or as described	
	important for immune response	below) and	
	development. Exemplary	immunodeficiencies (e.g., as	
	assays for transcription	described below). Preferred	
	through the GATA3 response	indications include neoplastic	
	element that may be used or	diseases (e.g., leukemia,	
	routinely modified to test	lymphoma, melanoma,	
	GATA3-response element	prostate, breast, lung, colon,	
	activity of polypeptides of the	pancreatic, esophageal,	
	invention (including antibodies	stomach, brain, liver, and	
	and agonists or antagonists of	urinary tract cancers and/or as	
	the invention) include assays	described below under	
	disclosed in Berger et al., Gene	"Hyperproliferative	
	66:1-10 (1998); Cullen and	Disorders"). Other preferred	
	Malm, Methods in Enzymol	indications include benign	
	216:362-368 (1992); Henthorn	dysproliferative disorders and	
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such	
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,	•
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.	
	Quant Biol 64:563-571 (1999);	Preferred indications include	
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,	
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,	
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,	
	Cell 89(4):587-596 (1997); and	acute lymphocytic anemia	
	Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,	
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's	
	contents of each of which are	lymphoma, arthritis, AIDS,	

				herein incorporated by	granulomatous disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
-				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
	_			1 cell line, which is an	meningitis, and Lyme Disease.
-	_			immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HSAWZ41	795	Activation of	This reporter assay measures	Highly preferred indications
	_		transcription	activation of the NFAT	include allergy, asthma, and
-	_		through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
_				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").

_						_				_																			_	
Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,
polypeptides of the invention	including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-	16338 (1995), and Turner et
			-								-																			
														-																
	_																													

i				al., J Exp Med 188:527-537 (1998), the contents of each of	granulomatous disease, inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
			r	by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
_				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
-				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
	****			many characteristics of	
				immature mast cells.	
/SH	HSAWZ41	795	Activation of	Assays for the activation of	A preferred embodiment of
_			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune

in growth and upregulate the	Activity", "Blood-Related
function of growth-related	Disorders", and/or
genes in many cell types.	"Cardiovascular Disorders"),
 Exemplary assays for	Highly preferred indications
 transcription through the SRE	include autoimmune diseases
that may be used or routinely	(e.g., rheumatoid arthritis,
modified to test SRE activity	systemic lupus erythematosis,
of the polypeptides of the	Crohn"s disease, multiple
invention (including antibodies	sclerosis and/or as described
and agonists or antagonists of	below), immunodeficiencies
the invention) include assays	(e.g., as described below),
disclosed in Berger et al., Gene	
66:1-10 (1998); Cullen and	immune response, and
Malm, Methods in Enzymol	suppressing a T cell-mediated
216:362-368 (1992); Henthorn	immune response. Additional
et al., Proc Natl Acad Sci USA	highly preferred indications
85:6342-6346 (1988); Benson	include inflammation and
et al., J Immunol 153(9):3862-	inflammatory disorders, and
3873 (1994); and Black et al.,	treating joint damage in
Virus Genes 12(2):105-117	patients with rheumatoid
(1997), the content of each of	arthritis. An additional highly
which are herein incorporated	preferred indication is sepsis.
by reference in its entirety. T	Highly preferred indications
cells that may be used	include neoplastic diseases
according to these assays are	(e.g., leukemia, lymphoma,
 publicly available (e.g.,	and/or as described below
through the ATCC).	under "Hyperproliferative
Exemplary T cells that may be	Disorders"). Additionally,
 used according to these assays	highly preferred indications
include the NK-YT cell line,	include neoplasms and
which is a human natural killer	cancers, such as, for example,

cell line with cytolytic and	leukemia, lymphoma,
cytotoxic activity.	melanoma, glioma (e.g.,
	malignant glioma), solid
	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	Preferred indications include
	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	arthritis, AIDS, granulomatous
	disease, inflammatory bowel
	disease, neutropenia,
	neutrophilia, psoriasis,
	suppression of immune
	reactions to transplanted
	organs and tissues, hemophilia,
	hypercoagulation, diabetes
	mellitus, endocarditis,
	meningitis, Lyme Disease,
	cardiac reperfusion injury, and

					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
SH	4SAWZ41	795	SEAP in OE-21		
HS	HSAWZ41	795	Activation of	Assays for the activation of	Highly preferred indications
			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
			,	involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
				assays for transcription	esophageal, stomach, brain,
				through the GAS response	liver and urinary cancer. Other
				element that may be used or	preferred indications include
	-			routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
				and agonists or antagonists of	metaplasia, and/or dysplasia.
				the invention) include assays	Preferred indications include
				disclosed in Berger et al., Gene	autoimmune diseases (e.g.,

rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia.
66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the SUPT cell line, that	may be used according to these	assays are publicly available	(e.g., through the ATCC).														
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					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
•					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HSAWZ41	795	Activation of	Assays for the activation of	A highly preferred
			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
			response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
				agonists or antagonists of the	described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,

	through the STAT6 response	rheumatoid arthritis, systemic
	element that may be used or	lupus erythematosis, multiple
	routinely modified to test	sclerosis and/or as described
	STAT6 response element	below) and
	activity of the polypeptides of	immunodeficiencies (e.g., as
	the invention (including	described below).
	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	"Hyperproliferative
	368 (1992); Henthorn et al.,	Disorders"). Preferred
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
 -	et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	(1998); Moffatt et al.,	prostate, breast, lung, colon,
	Transplantation 69(7):1521-	pancreatic, esophageal,
	1523 (2000); Curiel et al., Eur	stomach, brain, liver and
	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
	(1997); and Masuda et al., J	indications include benign
	Biol Chem 275(38):29331-	dysproliferative disorders and
	29337 (2000), the contents of	pre-neoplastic conditions, such
	each of which are herein	as, for example, hyperplasia,
	incorporated by reference in its	metaplasia, and/or dysplasia.
	entirety. T cells that may be	Preferred indications include
	used according to these assays	anemia, pancytopenia,
	are publicly available (e.g.,	leukopenia, thrombocytopenia,
	through the ATCC).	Hodgkin's disease, acute
	Exemplary T cells that may be	lymphocytic anemia (ALL),
	used according to these assays	plasmacytomas, multiple

			include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
HSAXA83	962	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

"Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases	(e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple selerosis and/or as described	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated	immune response, and suppressing a T cell-mediated immune response. Additional	highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in natients with rheumatoid	arthritis. An additional highly preferred indication is sepsis.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below	under "Hyperproliferative Disorders"). Additionally, highly preferred indications	include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g.,
SRE that may be used or routinely modified to test SRE activity of the polypeptides of	the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in	Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-	368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and	Black et al., Virus Genes 12(2):105-117 (1997), the	content of each of which are herein incorporated by reference in its entirety. T	cells that may be used according to these assays are	publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these	assays include the CTLL cell line, which is an IL-2 dependent suspension culture	or 1 cells with cytotoxic activity.
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				is infection (e.g., an infectious disease as described below
HSAYB43	797	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
		Apoptosis	caspase apoptosis are well known in the art and may be	embodiment of the invention includes a method for
			used or routinely modified to	stimulating endothelial cell
			assess the ability of	growth. An alternative highly
			polypeptides of the invention	preferred embodiment of the
			including antibodies and	invention includes a method
			agonists or antagonists of the	for inhibiting endothelial cell
			invention) to promote caspase	growth. A highly preferred
			protease-mediated apoptosis.	embodiment of the invention
			Induction of apoptosis in	includes a method for
			endothelial cells supporting the	stimulating endothelial cell
			vasculature of tumors is	proliferation. An alternative
			associated with tumor	highly preferred embodiment
			regression due to loss of tumor	of the invention includes a
			blood supply. Exemplary	method for inhibiting
			assays for caspase apoptosis	endothelial cell proliferation.
			that may be used or routinely	A highly preferred
			modified to test capase	embodiment of the invention
			apoptosis activity of	includes a method for
			polypeptides of the invention	stimulating apoptosis of
			(including antibodies and	endothelial cells. An
			agonists or antagonists of the	alternative highly preferred
			invention) include the assays	embodiment of the invention
			disclosed in Lee et al., FEBS	includes a method for
			Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
			Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
			209-218 (2000); and Karsan	A highly preferred

embodiment of the invention includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hvnertronhv myocardial
and Harlan, J Atheroscier Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine	aortic endothelial cells	(bAEC), which are an example	of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.										
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infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders")	Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect wessels	such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly	preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or	Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders.	Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary

angiomatosis, hernangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urnary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other												
	angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also include cancers such as,	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary cancer. Preferred indications include benign	pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,	such as, atherosclerosis, hypertension, coronary artery	disease, inflammatory vasculitides, Reynaud's disease and Reynaud's	phenomenom, aneurysms, restenosis; venous and	lymphatic disorders such as thrombophlebitis, lymphanoitis, and	lymphedema; and other vascular disorders such as
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peripheral vascular disease,	and cancer. Highly	ij	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.
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				Preferred indications include
				blood disorders (e.g., as
				described below under
				"Immune Activity", "Blood-
				Related Disorders", and/or
				"Cardiovascular Disorders").
		-		Preferred indications include
				autoimmune diseases (e.g.,
				rheumatoid arthritis, systemic
				lupus erythematosis, multiple
				sclerosis and/or as described
				below) and
				immunodeficiencies (e.g., as
	-			described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HSDEK49	862	Activation of	Assays for the activation of	A preferred embodiment of
		transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as T-cells).	routinely modified to assess	preferred embodiment of the
			the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
			antibodies and agonists or	increasing) TNF alpha

production. Preferred indications include blood disorders (e.g., as described	below under "Immune Activity", "Blood-Related Disorders" and/or	"Cardiovascular Disorders"), Highly preferred indications	include autoimmune diseases	systemic lupus erythematosis,	Crohn's disease, multiple sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,		under "Hyperproliferative
antagonists of the invention) to regulate the serum response factors and modulate the	expression of genes involved in growth. Exemplary assays	SRE that may be used or	activity of the polypeptides of	antibodies and agonists or	antagonists of the invention)	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell
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		line, which is an IL-2	Disorders"). Additionally,
		dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
	8	activity.	cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
<u>-</u>			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
-			example, hyperplasia,
			metaplasia, and/or dysplasia.
-			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
_			lymphocytic anemia (ALL),
			plasmacytomas, multiple
			myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues

,				hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HSDEK49	798	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,

	used or routinely modified to	nodified to	hyperosmolar coma.
	test for regulation of	of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	alic Enzyme	heart disease, atherosclerosis,
	(in adipoocytes) by		microvascular disease,
	polypeptides of the invention	invention	hypertension, stroke, and other
	(including antibodies and	ies and	diseases and disorders as
	agonists or antagonists of the	nists of the	described in the
	invention) include assays	assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	per, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	1,	endocrine disorders (as
	12(11):1778-91 (1998);	998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	, et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	5):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	berg, A., et	wound healing, and infection
	al., J Biol Chem,		(e.g., infectious diseases and
_	272(32):20108-20117 (1997);	117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	e 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	n, B., et al.,	below, especially of the
	Methods in Enzymol.	iol.	urinary tract and skin), carpal
	216:362–368 (1992), the	2), the	tunnel syndrome and
	contents of each of which is	f which is	Dupuytren's contracture).
	herein incorporated by	d by	An additional highly preferred
	reference in its entirety.	irety.	indication is obesity and/or
	Hepatocytes that may be used	nay be used	complications associated with
	according to these assays are	assays are	obesity. Additional highly
	publicly available (e.g.,	(e.g.,	preferred indications include
	through the ATCC) and/or) and/or	weight loss or alternatively,
	may be routinely generated.	enerated.	weight gain. Aditional
	Exemplary hepatocytes that	cytes that	highly preferred indications are

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complications associated with insulin resistance.		A highly preferred	indication is diabetes mellitus.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other
may be used according to these assays includes the H4IIE rat liver hepatoma cell line.		Assays for the regulation of	transcription through the	PEPCK promoter are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to activate the	PEPCK promoter in a reporter	construct and regulate liver	gluconeogenesis. Exemplary	assays for regulation of	transcription through the	PEPCK promoter that may be	used or routinely modified to	test for PEPCK promoter	activity (in hepatocytes) of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn
	MIP-1a in HMC	Regulation of	transcription	through the PEPCK	promoter in	hepatocytes																						
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	HSDEK49	HSDFJ26							-			-																
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		et al Proc Natl Acad Sci USA	diseases and disorders as
			described in the
		03.0342-0340 (1700), I atherd of all Dishotes	"Conditional In the Disorders"
		Locillead et al., Diabetes	Calulovasculal Disolucis
		49(6):896-903 (2000); and	section below), dyslipidemia,
		Yeagley et al., J Biol Chem	endocrine disorders (as
		275(23):17814-17820 (2000),	described in the "Endocrine
		the contents of each of which	Disorders" section below),
	-	is herein incorporated by	neuropathy, vision impairment
		reference in its entirety.	(e.g., diabetic retinopathy and
		Hepatocyte cells that may be	blindness), ulcers and impaired
		used according to these assays	wound healing, infection (e.g.,
		are publicly available (e.g.,	an infectious diseases or
		through the ATCC) and/or	disorders as described in the
		may be routinely generated.	"Infectious Diseases" section
		Exemplary liver hepatoma	below, especially of the
		cells that may be used	urinary tract and skin), carpal
		according to these assays	tunnel syndrome and
		include H4lle cells, which	Dupuytren's contracture).
		contain a tyrosine amino	An additional highly preferred
-		transferase that is inducible	indication is obesity and/or
		with glucocorticoids, insulin,	complications associated with
		or cAMP derivatives.	obesity. Additional highly
			preferred indications include
			weight loss or alternatively,
			weight gain. Additional
			highly preferred indications are
			complications associated with
			insulin resistance.
			Additional highly preferred
			indications are disorders of the
			musculoskeletal systems

A de in A Di A de in A Di A de in A de	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell orowth A highly preferred
	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
	Protection from Endothelial Cell Apoptosis.
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		inhihit caspase protease-	embodiment of the invention
		mediated apoptosis.	includes a method for
		Exemplary assays for caspase	stimulating endothelial cell
		apoptosis that may be used or	proliferation. An alternative
		routinely modified to test	highly preferred embodiment
		caspase apoptosis rescue of	of the invention includes a
		polypeptides of the invention	method for inhibiting
-		(including antibodies and	endothelial cell proliferation.
_		agonists or antagonists of the	A highly preferred
		invention) include the assays	embodiment of the invention
		 disclosed in Romeo et al.,	includes a method for
		Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
		(2000); Messmer et al., Br J	growth. An alternative highly
		Pharmacol 127(7): 1633-1640	preferred embodiment of the
		 (1999); and J Atheroscler	invention includes a method
		Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
		 the contents of each of which	growth. A highly preferred
_		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
		 Endothelial cells that may be	stimulating apoptosis of
	•	 used according to these assays	endothelial cells. An
	-	 are publicly available (e.g.,	alternative highly preferred
		through commercial sources).	embodiment of the invention
		Exemplary endothelial cells	includes a method for
		that may be used according to	inhibiting (e.g., decreasing)
		these assays include bovine	apoptosis of endothelial cells.
		aortic endothelial cells	A highly preferred
		 (bAEC), which are an example	embodiment of the invention
		of endothelial cells which line	includes a method for
		blood vessels and are involved	stimulating angiogenisis. An
		in functions that include, but	alternative highly preferred

embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a	method for reducing cardiac hypertrophy. An alternative highly preferred embodiment	of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as described below under "Hypernroliferative	Disorders"), and disorders of the cardiovascular system	(e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,	cardiomyopathy, valvular regurgitation, left ventricular	dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac	infarction, chronic	hemodynamic overload, and/or as described below under	"Cardiovascular Disorders").
are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.											
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Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,
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lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as atherosclerosis.	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis,	lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as
\(\frac{1}{2}\) \(\frac{1}2\) \(\frac{1}2\) \(\frac{1}2\) \(\frac{1}2\) \(\frac{1}2\) \(\frac{1}2\) \(\frac{1}			Zi, v q a q ii

wounds, burns, and injured tissue (e.g., vascular injury	such as, injury resulting from balloon angioplasty, and	atheroschlerotic lesions), implant fixation, scarring.	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related
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described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infections Diseases" section
reporter construct (such as that	containing the GLUT4	promoter) and to regulate	insulin production. The	DMEF1 response element is	present in the GLUT4	promoter and binds to MEF2	transcription factor and another	transcription factor that is	required for insulin regulation	of Glut4 expression in skeletal	muscle. GLUT4 is the primary	insulin-responsive glucose	transporter in fat and muscle	tissue. Exemplary assays that	may be used or routinely	modified to test for DMEF1	response element activity (in	adipocytes and pre-adipocytes)	by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed inThai, M.V., et al., J	Biol Chem, 273(23):14285-92	(1998); Mora, S., et al., J Biol	Chem, 275(21):16323-8	(2000); Liu, M.L., et al., J Biol	Chem, 269(45):28514-21	(1994); "Identification of a 30-	hase pair regulatory element
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below, especially of the urinary tract and skin). An additional highly preferred	indication is obesity and/or complications associated with	obesity. Additional highly	preferred indications include	weight gain. Additional highly	preferred indications are	complications associated with	insulin resistance.																			
and novel DNA binding protein that regulates the	transgenic mice", J Biol Chem. 2000 Aug 4:275(31):23666-73:	Berger, et al., Gene 66:1-10	(1988); and, Cullen, B., et al.,	Methods in Enzymol. 216:362–368 (1992), the	contents of each of which is	herein incorporated by	reference in its entirety.	Adipocytes and pre-adipocytes	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the mouse 3T3-L1 cell	line which is an adherent	mouse preadipocyte cell line.	Mouse 3T3-L1 cells are a	continuous substrain of 3T3	fibroblasts developed through	clonal isolation. These cells	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	1, 1,1,1
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microvascular disease, hypertension, stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired	wound healing, and infection (e.g., infectious diseases and disorders as described in the	"Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dimitten's contracture)	Additional highly preferred indications are complications associated with insulin resistance.	
response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Reusch et al., Mol Cell Biol	20(3):1008-1020 (2000); and Klemm et al., J Biol Chem 273:917-923 (1998), the	contents of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used	according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte	cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed
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85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.					Proc Natl Acad Sci USA	confusion, drowsiness,
Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Pre- adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 313-L1 cells. 373-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 373 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. 801 SEAP in AIR Phos C2C12 Assays for the activation of transcription transcription transcription CSRT) are well-known in the					85:6342-6346 (1988); and	nonketotic hyperglycemic-
12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion undergo appropriate differentiation conditions known in the art. 801 SEAP in AIR Phos C2C12 Assays for the activation of transcription through the through serum response Element in (SRE) are well-known in the					Black et al., Virus Genes	hyperosmolar coma,
content of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Activation of transcription through the transcription transcription CSRE) are well-known in the					12(2):105-117 (1997), the	cardiovascular disease (e.g.,
reference in its entirety. Preadipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Activation of transcription through the transcription transcription CSRE) are well-known in the					content of each of which are	heart disease, atherosclerosis,
adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Assays for the activation of transcription through the through serum Serum Response Element in (SRE) are well-known in the					herein incorporated by	microvascular disease,
adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Assays for the activation of transcription through the through serum Serum Response Element Serum Response Element Serum Response Element Serum Response Element					reference in its entirety. Pre-	hypertension, stroke, and other
according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. 801 SEAP in Alk Phos C2C12 Assays for the activation of transcription through the through serum Serum Response Element in (SRE) are well-known in the					adipocytes that may be used	diseases and disorders as
publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Assays for the activation of transcription through the through serum Serum Response Element in (SRF) are well-known in the					according to these assays are	described in the
through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Assays for the activation of transcription transcription Serum Response Element Serum RSRF) are well-known in the					publicly available (e.g.,	"Cardiovascular Disorders"
Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Assays for the activation of transcription transcription Serum Response Element in (SRE) are well-known in the					through the ATCC) and/or	section below), dyslipidemia,
Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Assays for the activation of transcription transcription transcription Serum Response Element response element in (SRE) are well-known in the					may be routinely generated.	endocrine disorders (as
cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. 801 SEAP in Alk Phos C2C12 Activation of Assays for the activation of transcription through the through serum Serum Response Element SRED are well-known in the					Exemplary mouse adipocyte	described in the "Endocrine
according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. 801 SEAP in Alk Phos C2C12 Activation of Assays for the activation of transcription through serum Serum Response Element SRE) are well-known in the					cells that may be used	Disorders" section below),
include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 Assays for the activation of transcription transcription of transcription through the through serum Serum Response Element (SRE) are well-known in the	_				according to these assays	neuropathy, vision impairment
is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art. SEAP in Alk Phos C2C12 801 Activation of Assays for the activation of transcription transcription transcription (SRF) are well-known in the					include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
preadipocyte cell line that is a continuous substrain of 3T3 (e. fibroblast cells developed dii through clonal isolation and "In undergo a pre-adipocyte to adipose-like conversion under prappropriate differentiation conditions known in the art. in condition of transcription of transcription of transcription of transcription (SRE) are well-known in the response element in (SRE) are well-known in the response element in the continuous substrain of through serum (SRE) are well-known in the response element in the continuous element in the response element in the response element in the continuous element in the continuo					is an adherent mouse	blindness), ulcers and impaired
fibroblast cells developed distribution and through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under prappropriate differentiation conditions known in the art. in conditions known in the conversion of transcription transc					preadipocyte cell line that is a	wound healing, and infection
fibroblast cells developed dithrough clonal isolation and through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under prappropriate differentiation conditions known in the art. in cachination of transcription of transcription of transcription (SRE) are well-known in the response element in (SRE) are well-known in the response element in the response conditions and conditions are supported by the conversion of the conversion of the conditions and conditions are supported by the conversion of the conversion and conditions are conditions and conditions are conditions.					continuous substrain of 3T3	(e.g., infectious diseases and
through clonal isolation and undergo a pre-adipocyte to be adipose-like conversion under prappropriate differentiation conditions known in the art. in SEAP in Alk Phos C2C12 801 Activation of Assays for the activation of transcription through serum Serum Response Element merchange element in (SRE) are well-known in the response element in the response element in the response are series and series and series are series and series and series and series are					fibroblast cells developed	disorders as described in the
adipose-like conversion under pradipocyte to adipose-like conversion under prappropriate differentiation co-conditions known in the art. in C2C12 801 SEAP in Alk Phos C2C12 801 Activation of Assays for the activation of transcription transcription through serum Serum Response Element maresponse element in (SRE) are well-known in the response element in the response adil-known in the response element in the adil-known in the adil-kno					through clonal isolation and	"Infectious Diseases" section
adipose-like conversion under prappropriate differentiation conditions known in the art. in SEAP in Alk Phos C2C12 801 Activation of Assays for the activation of transcription through serum Serum Response Element meresponse element in (SRE) are well-known in the response response element in the response response element in the response appropriate differentiation conditions appropriate differentiation condition conditions appropriate differentiation condition condition condition					undergo a pre-adipocyte to	below). Additional highly
801 SEAP in Alk Phos C2C12 801 Activation of transcription through serum through serum transcription tresponse element in (SRE) are well-known in the part.					adipose-like conversion under	preferred indications are
801 SEAP in Alk Phos C2C12 801 Activation of Assays for the activation of transcription through serum Response Element mercan response element in (SRE) are well-known in the response to the activation of the serious conditions are serious conditions.					appropriate differentiation	complications associated with
801 SEAP in Alk Phos C2C12 801 Activation of transcription through serum through serum (SRE) are well-known in the response element in (SRE) are well-known in the response to the series of the serie					conditions known in the art.	insulin resistance.
801 Activation of Assays for the activation of transcription transcription through the through serum Serum Response Element m response element in (SRE) are well-known in the re-		HSDSB09	801	SEAP in Alk Phos C2C12		
transcription through the Serum Response Element (SRE) are well-known in the		HSDSB09	801	Activation of	Assays for the activation of	A preferred embodiment of
Serum Response Element (SRE) are well-known in the				transcription	transcription through the	the invention includes a
(SRE) are well-known in the				through serum	Serum Response Element	method for inhibiting (e.g.,
(DIC) are then hard in miles				response element in	(SRE) are well-known in the	reducing) TNF alpha

immune cells (such	art and may be used or	production. An alternative
as T-cells).	routinely modified to assess	preferred embodiment of the
	the ability of polypeptides of	invention includes a method
	the invention (including	for stimulating (e.g.,
	antibodies and agonists or	increasing) TNF alpha
	antagonists of the invention) to	production. Preferred
	regulate the serum response	indications include blood
	factors and modulate the	disorders (e.g., as described
	expression of genes involved	below under "Immune
	in growth. Exemplary assays	Activity", "Blood-Related
	for transcription through the	Disorders", and/or
 	SRE that may be used or	"Cardiovascular Disorders"),
	routinely modified to test SRE	Highly preferred indications
-	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
	antagonists of the invention)	Crohn's disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
 	(1998); Cullen and Malm,	(e.g., as described below),
	Methods in Enzymol 216:362-	boosting a T cell-mediated
 -	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.

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III. and formed indications	anons	eases	10ma,	ylow	ntive	ıally,	highly preferred indications	þ	cancers, such as, for example,		.;	pile	tumors, and prostate, breast,	ڻ ٽ	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	'e	disorders and pre-neoplastic)r	•	metaplasia, and/or dysplasia.	Preferred indications include	ۍـ	leukopenia, thrombocytopenia,	ute	lymphocytic anemia (ALL),	iple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	v bowe
المنا ال)	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	d indic	include neoplasms and	s, for e	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	state,	lung, colon, pancreatic,	mach,	y canc	ations	benign dysproliferative	re-neo	conditions, such as, for	example, hyperplasia,	l'or dy	ations	anemia, pancytopenia,	omboc	Hodgkin's disease, acute	emia (plasmacytomas, multiple	citt's ly	, grant	mator
96	וכוכווכ	eoplas	kemia,	descri	yperpi	s"). A	eferre	eoplas	such a	, lymp	ia, glio	it glior	and pro	on, pai	al, sto	urina	indica	ysprol	and p	ıs, suc	, hypei	ia, and	l indic	pancyt	iia, thr	's dise	ytic ar	ytomas	a, Burk	AIDS	inflam
145	giiry pi	lude n	g., leul	d/or as	der "H	sorder	ghly pr	lude n	ncers,	ıkemia	lanom	ılignar	nors, a	lg, col	phage	er and	eferred	nign d	sorders	ndition	ample	etaplas	eferred	emia, j	akoper	odgkin	mphoc	asmac	yeloma	thritis,	disease, inflammatory bowel
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ļ			Exemplary mouse T cells that	may be used according to these	L cell		dependent suspension culture	ပ																							
	; (c.g.,	(j	e T cel	ording	e CTL	IL-2	sion c	totoxi																							
11-11	عالقاله/	e ATC	mous,	ed acc	ude th	ı is an	susper	with cy																							
	publicity available (e.g.,	through the ATCC)	mplary	be use	assays include the CTLL cell	line, which is an IL-2	endent	of T cells with cytotoxic	activity.	•																					
	and	thro	Exe	may	assa	line	deb	ofT	activ																						
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disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,
	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements
	Regulation of transcription of Malic Enzyme in adipocytes
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	HSDSB09

putative PPAR response	impotence (e.g., due to diabetic
elements. ME promoter may	neuropathy or blood vessel
also responds to AP1 and other	blockage), seizures, mental
transcription factors.	confusion, drowsiness,
Exemplary assays that may be	nonketotic hyperglycemic-
used or routinely modified to	hyperosmolar coma,
test for regulation of	cardiovascular disease (e.g.,
transcription of Malic Enzyme	heart disease, atherosclerosis,
(in adipoocytes) by	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in: Streeper, R.S., et	section below), dyslipidemia,
al., Mol Endocrinol,	endocrine disorders (as
12(11):1778-91 (1998);	described in the "Endocrine
Garcia-Jimenez, C., et al., Mol	Disorders" section below),
Endocrinol, 8(10):1361-9	neuropathy, vision impairment
(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
Biol Chem, 274(25):17997-	blindness), ulcers and impaired
8004 (1999); Ijpenberg, A., et	wound healing, and infection
al., J Biol Chem,	(e.g., infectious diseases and
272(32):20108-20117 (1997);	disorders as described in the
Berger, et al., Gene 66:1-10	"Infectious Diseases" section
 (1988); and, Cullen, B., et al.,	below, especially of the
Methods in Enzymol.	urinary tract and skin), carpal
216:362–368 (1992), the	tunnel syndrome and
contents of each of which is	Dupuytren's contracture).
herein incorporated by	An additional highly preferred
reference in its entirety.	indication is obesity and/or
Hepatocytes that may be used	complications associated with

			according to these assays are publicly available (e.g.,	obesity. Additional highly preferred indications include weight loss or alternatively
			may be routinely generated.	weight gain. Aditional
			Exemplary hepatocytes that	highly preferred indications are
			may be used according to these	complications associated with
			assays includes the H4IIE rat	insulin resistance.
			liver hepatoma cell line.	
HSDSB09	801	SEAP in HIB/CRE		
60BSQSH	801	Stimulation of	Assays for measuring calcium	A highly preferred
		Calcium Flux in	flux are well-known in the art	indication is diabetes mellitus.
		pancreatic beta	and may be used or routinely	An additional highly preferred
		cells.	modified to assess the ability	indication is a complication
			of polypeptides of the	associated with diabetes (e.g.,
			invention (including antibodies	diabetic retinopathy, diabetic
			and agonists or antagonists of	nephropathy, kidney disease
			the invention) to mobilize	(e.g., renal failure,
			calcium. For example, the	nephropathy and/or other
			FLPR assay may be used to	diseases and disorders as
			measure influx of calcium.	described in the "Renal
			Cells normally have very low	Disorders" section below),
			concentrations of cytosolic	diabetic neuropathy, nerve
			calcium compared to much	disease and nerve damage
			higher extracellular calcium.	(e.g., due to diabetic
			Extracellular factors can cause	neuropathy), blood vessel
			an influx of calcium, leading to	blockage, heart disease, stroke,
			activation of calcium	impotence (e.g., due to diabetic
			responsive signaling pathways	neuropathy or blood vessel
			and alterations in cell	blockage), seizures, mental
			functions. Exemplary assays	confusion, drowsiness,
			that may be used or routinely	nonketotic hyperglycemic-

modified to measure calcium	hyperosmolar coma,
flux by polypeptides of the	cardiovascular disease (e.g.,
 invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Satin LS, et al.,	diseases and disorders as
Endocrinology, 136(10):4589-	described in the
601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
Endocrinology, 136(7):2960-6	section below), dyslipidemia,
(1995); Richardson SB, et al.,	endocrine disorders (as
Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
(1992); and, Meats, JE, et al.,	Disorders" section below),
Cell Calcium 1989 Nov-	neuropathy, vision impairment
Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
contents of each of which is	blindness), ulcers and impaired
herein incorporated by	wound healing, and infection
reference in its entirety.	(e.g., infectious diseases and
 Pancreatic cells that may be	disorders as described in the
used according to these assays	"Infectious Diseases" section
are publicly available (e.g.,	below, especially of the
through the ATCC) and/or	urinary tract and skin), carpal
 may be routinely generated.	tunnel syndrome and
Exemplary pancreatic cells that	Dupuytren's contracture).
may be used according to these	
assays include HITT15 Cells.	indication is obesity and/or
HITT15 are an adherent	complications associated with
 epithelial cell line established	obesity. Additional highly
from Syrian hamster islet cells	preferred indications include
 transformed with SV40. These	weight loss or alternatively,
cells express glucagon,	weight gain. Aditional
somatostatin, and	highly preferred indications are

complications associated with insulin resistance.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described
glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate	expression of mast cell genes
	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	
	801	
	HSDSB09	

below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune
important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	[14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,
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			through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an	reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
			immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells	
HSDSB09	801	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
			invention) to regulate NFA1 transcription factors and	lupus erythematosis, multiple sclerosis and/or as described

modulate expression of genes	below) and
 involved in	immunodeficiencies (e.g., as
immunomodulatory functions.	described below). Preferred
Exemplary assays for	indications include neoplastic
transcription through the	diseases (e.g., leukemia,
 NFAT response element that	lymphoma, melanoma,
may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
 (including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
 Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
 85:6342-6346 (1988); De Boer	Preferred indications include
 et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al., J Exp Med 188:527-537	granulomatous disease,
(1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,
Mast cells that may be used	suppression of immune

systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".									
transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Stassen	et al, J Immunol 166(7):4391-8	(2001); and Marquardt and	Walker, J Allergy Clin	Immunol 105(3):500-5 (2000),	the contents of each of which	are herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells

			that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	
HSDSB09	801	Activation of transcription through STAT6 response element in immune cells (such as mast cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element in immune cells (such as in the human HMC-1 mast cell line) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies	Highly preferred indications include allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include hematopoietic and immunological disorders (e.g.,
			and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription through the STAT6 response element that may be used or routinely modified to test STAT6 response element	as described below under "Immune Activity", "Blood- Related Disorders", and/or "Cardiovascular Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as

activity of the polypeptides of described below). Preferred	or	antagonists of the invention) lymphoma, melanoma, and/or	include assays disclosed in as described below under	Berger et al., Gene 66:1-10 "Hyperproliferative	(1998); Cullen and Malm, Disorders"). Preferred	Methods in Enzymol 216:362- indications include neoplasms	368 (1992); Henthorn et al., and cancer, such as, for	85:6342-6346 (1988); melanoma, and prostate,	Sherman, Immunol Rev breast, lung, colon, pancreatic,	179:48-56 (2001); Malaviya esophageal, stomach, brain,	and Uckun, J Immunol liver and urinary cancer. Other	168:421-426 (2002); Masuda preferred indications include	et al., J Biol Chem benign dysproliferative	(37 (2000);	and Masuda et al., J Biol Chem conditions, such as, for	 contents of each of which are metaplasia, and/or dysplasia.	herein incorporated by Preferred indications include	reference in its entirety. Mast hematopoietic and	cells that may be used immunological disorders such	according to these assays are as arthritis, AIDS,	publicly available (e.g., granulomatous disease,	through the ATCC). inflammatory bowel disease,	nast cells	that may be used according to neutrophilia, psoriasis,	these assays include the HMC- suppression of immune	1 cell line, which is an reactions to transplanted	
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nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Aditional
test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,	138(9):3735-40 (1997); Kim,	K.H., et al., FEBS Lett,	377(2):237-9 (1995); and,	Miraglia S et. al., Journal of	Biomolecular Screening,	4:193-204 (1999), the contents	of each of which is herein	incorporated by reference in its	entirety. Pancreatic cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC)	and/or may be routinely	generated. Exemplary	pancreatic cells that may be	used according to these assays	include rat INS-1 cells. INS-1	cells are a semi-adherent cell	line established from cells	isolated from an X-ray induced	rat transplantable insulinoma.
			_																					_						

l of native complications associated with including insulin resistance. S: Asfari 1992			u812 e. n of e trare nd may diffied antion nd of the FKB I	(e.g., rheumatoid arthritis, the
These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.		at/IL4 tiCD3		Exemplary assays for transcription through the
	801 SEAP in Jurkat/IL4 promoter	801 SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	4 Activation of transcription through NFKB response element in immune cells (such as basophils).	
	HSDSB09	HSDSB09	HSDSB09	

multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".										
NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Basophils that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally	established from a patient with	chronic myelogenous	leukemia. It is an immature	prebasophilic cell line that can
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				be induced to differentiate into	
H	HSDSB09	801	SEAP in		
			Synergy)		
HS	HSDSB09	801	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
	-		response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
_			_	antagonists of the invention) to	production. Preferred
	-			regulate serum response	indications include blood
_				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
	***************************************			genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
<u>.</u>				of the polypeptides of the	Crohn"s disease, multiple
	-			invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and

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suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in patients with rheumatoid	arthritis. An additional highly preferred indication is sepsis.	include neoplastic diseases	and/or as described below	under "Hyperproliferative Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, Iympnoma, melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metanlasia and/or dysnlasia
Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of which are herein incorporated	cells that may be used	publicly available (e.g.,	through the ATCC). Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cytotoxic activity.						·					
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				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
	_			Hodgkin's disease, acute
•			-	lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
_				arthritis, AIDS, granulomatous
				disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues, hemophilia,
				hypercoagulation, diabetes
				mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
_				is infection (e.g., an infectious
				disease as described below
00000011	100			under "Infectious Disease").
HSDSB09	801	Activation of	Assays for the activation of	A highly preferred
		transcription	transcription through the	indication is allergy.
		through STAT6	Signal Transducers and	Another highly preferred
		response element in	Activators of Transcription	indication is asthma.
		immune cells (such	(STAT6) response element are	Additional highly preferred
		as T-cells).	well-known in the art and may	indications include
			be used or routinely modified	inflammation and
_			to assess the ability of	in flowing to me discount

	polypeptides of the invention	Preferred indications include
	(including antibodies and	blood disorders (e.g., as
	agonists or antagonists of the	described below under
	invention) to regulate STAT6	"Immune Activity", "Blood-
	transcription factors and	Related Disorders", and/or
	modulate the expression of	"Cardiovascular Disorders").
	multiple genes. Exemplary	Preferred indications include
	assays for transcription	autoimmune diseases (e.g.,
	through the STAT6 response	rheumatoid arthritis, systemic
	element that may be used or	lupus erythematosis, multiple
	routinely modified to test	sclerosis and/or as described
	STAT6 response element	below) and
-	activity of the polypeptides of	immunodeficiencies (e.g., as
	the invention (including	described below).
	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	"Hyperproliferative
	368 (1992); Henthorn et al.,	Disorders"). Preferred
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
	et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	(1998); Moffatt et al.,	prostate, breast, lung, colon,
	Transplantation 69(7):1521-	pancreatic, esophageal,
	1523 (2000); Curiel et al., Eur	stomach, brain, liver and
	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
	(1997); and Masuda et al., J	indications include benign
	Biol Chem 275(38):29331-	dysproliferative disorders and
	29337 (2000), the contents of	pre-neoplastic conditions, such

			each of which are herein	as, for example, hyperplasia,
			entirety. T cells that may be	Inetaplasia, and/or dysplasia. Preferred indications include
			used according to these assays	anemia, pancytopenia,
			are publicly available (e.g.,	leukopenia, thrombocytopenia,
			through the ATCC).	Hodgkin's disease, acute
			Exemplary I cells that may be	lymphocytic anemia (ALL),
			used according to these assays	plasmacytomas, multiple
			include the SUPT cell line,	myeloma, Burkitt's lymphoma,
			which is a suspension culture	arthritis, AIDS, granulomatous
			of IL-2 and IL-4 responsive T	disease, inflammatory bowel
			cells.	disease, sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additional preferred
	-			indication is infection (e.g., an
				infectious disease as described
				below under "Infectious
				Disease").
HSDSB09	801	CXCR4 in SW480		
SDSE75	802	Myoblast cell	Assays for muscle cell	Highly preferred indications
		proliferation	proliferation are well known in	include diabetes, myopathy,
			the art and may be used or	muscle cell atrophy, cancers of
			routinely modified to assess	muscle (such as,
			the ability of polypeptides of	rhabdomyoma, and
			the invention (including	rhabdosarcoma),

antibodies and agonists or	cardiovascular disorders (such
antagonists of the invention) to	as congestive heart failure.
stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
cell proliferation. Exemplary	congenital cardiovascular
 assays for myoblast cell	abnormalities, heart disease,
proliferation that may be used	cardiac arrest, heart valve
 or routinely modified to test	disease, vascular disease, and
activity of polypeptides and	also as described below under
antibodies of the invention	"Cardiovascular Disorders"),
(including agonists or	stimulating myoblast
antagonists of the invention)	proliferation, and inhibiting
include, for example, assays	myoblast proliferation.
disclosed in: Soeta, C., et al.	•
"Possible role for the c-ski	
gene in the proliferation of	
myogenic cells in regenerating	
skeletal muscles of rats" Dev	
Growth Differ Apr;43(2):155-	
64 (2001); Ewton DZ, et al.,	
"IGF binding proteins-4, -5	
and -6 may play specialized	
roles during L6 myoblast	
 proliferation and	
 differentiation" J Endocrinol	
 Mar;144(3):539-53 (1995);	
and, Pampusch MS, et	
al., Effect of transforming	
growth factor beta on	
proliferation of L6 and	
embryonic porcine myogenic	
cells" J Cell Physiol	

			Jun;143(3):524-8 (1990); the	
			contents of each of which are	
			herein incorporated by	
			reference in their entirety.	
			Exemplary myoblast cells that	
			may be used according to these	
			assays include the rat myoblast	
			L6 cell line. Rat myoblast L6	
			cells are an adherent rat	
			myoblast cell line, isolated	
		-	from primary cultures of rat	
			thigh muscle, that fuse to form	
			multinucleated myotubes and	
			striated fibers after culture in	
			differentiation media.	
HSDSE75	805	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
			by T cells and has strong	embodiment of the invention
			effects on B cells. IL-6	includes a method for
			participates in IL-4 induced	stimulating (e.g., increasing)
			IgE production and increases	IL-6 production. An alternative
			IgA production (IgA plays a	highly preferred embodiment
			role in mucosal immunity).	of the invention includes a
			IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
			Deregulated expression of IL-6	reducing) IL-6 production. A
			has been linked to autoimmune	highly preferrred indication is
			disease, plasmacytomas,	the stimulation or enhancement
			myelomas, and chronic	of mucosal immunity. Highly
			hyperproliferative diseases.	preferred indications include
			Assays for immunomodulatory	blood disorders (e.g., as
			and differentiation factor	described below under
			proteins produced by a large	"Immune Activity", "Blood-

	variety of cells where the	Related Disorders", and/or
	expression level is strongly	"Cardiovascular Disorders"),
	regulated by cytokines, growth	and infection (e.g., as
	factors, and hormones are well	described below under
	known in the art and may be	"Infectious Disease"). Highly
	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
-	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under

	Biomole	193-	"Hyperproliferative
	204(199	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lympho	"Lymphocytes: a practical	indications include neoplasms
	approach	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); a	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immuno	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), t	(1997), the contents of each of	prostate, breast, lung, colon,
	which ar	which are herein incorporated	pancreatic, esophageal,
	by refere	by reference in its entirety.	stomach, brain, liver and
	Human	Human dendritic cells that may	urinary cancer. Other preferred
	pe nsed a	be used according to these	indications include benign
	assays m	assays may be isolated using	dysproliferative disorders and
	techniqu	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwis	otherwise known in the art.	as, for example, hyperplasia,
	Human	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen p	antigen presenting cells in	Preferred indications include
	suspension	suspension culture, which,	anemia, pancytopenia,
	when act	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cy	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregula	upregulate T cell proliferation	lymphocytic anemia (ALL),
	and func	and functional activities.	multiple myeloma, Burkitt's
			lymphoma, arthritis, AIDS,
			granulomatous disease,
			inflammatory bowel disease,
			sepsis, neutropenia,
			neutrophilia, psoriasis,
-			suppression of immune
			reactions to transplanted
			organs and tissues,
-			hemophilia, hypercoagulation,
			diabetes mellitus, endocarditis,

	11002062				meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
	HSDZK57	803	SEAP in Alk Phos C2C12		
	HSDZR57	803	SEAP in ATP-3T3- L1		
<u>.</u>	HSDZR57	803	Activation of	Kinase assay. JNK and p38	A highly preferred
			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred
				antibodies and agonists or	embodiment of the invention
				antagonists of the invention) to	includes a method for
				promote or inhibit cell	stimulating endothelial cell
_				proliferation, activation, and	proliferation. An alternative
•				apoptosis. Exemplary assays	highly preferred embodiment
				for JNK and p38 kinase	of the invention includes a
				activity that may be used or	method for inhibiting
_				routinely modified to test JNK	endothelial cell proliferation.
				and p38 kinase-induced	A highly preferred
,		•		activity of polypeptides of the	embodiment of the invention
				invention (including antibodies	includes a method for
				and agonists or antagonists of	stimulating apoptosis of

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endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a
the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	
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method for inducing cardiac hypertrophy. Highly preferred indications include	neoplasue diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of	the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension.	aortic stenosis, cardiomyopathy, valvular	regurgitation, left ventricular dysfunction, atherosclerosis	and atherosclerotic vascular disease, diabetic nephropathy,	hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under	"Cardiovascular Disorders").	Highly preferred indications include cardiovascular,	endothelial and/or angiogenic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels themselves, such as of the
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		and/or lymphatics). Highly
		preferred are indications that
		stimulate angiogenesis and/or
		cardiovascularization. Highly
		preferred are indications that
		inhibit angiogenesis and/or
		cardiovascularization.
		Highly preferred indications
		include antiangiogenic activity
		to treat solid tumors,
		leukemias, and Kaposi"s
		sarcoma, and retinal disorders.
		Highly preferred indications
		include neoplasms and cancer,
		such as, Kaposi"s sarcoma,
		hemangioma (capillary and
-		cavernous), glomus tumors,
		telangiectasia, bacillary
		angiomatosis,
		hemangioendothelioma,
		angiosarcoma,
		haemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
		preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
		indications include benign

dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud's	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal
										-																				

diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or	other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular	degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest,	vascular disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as

				described below). Additional
				preferred indications include
				inflammation and
				inflammatory disorders (such
-				as acute and chronic
				inflammatory diseases, e.g.,
				inflammatory bowel disease
				and Crohn's disease), and pain
				management.
HSIDJ81	804	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
			of insulin are well-known in	is diabetes mellitus. An
			the art and may be used or	additional highly preferred
			routinely modified to assess	indication is a complication
			the ability of polypeptides of	associated with diabetes (e.g.,
			the invention (including	diabetic retinopathy, diabetic
			antibodies and agonists or	nephropathy, kidney disease
			antagonists of the invention) to	(e.g., renal failure,
			stimulate insulin secretion.	nephropathy and/or other
			For example, insulin secretion	diseases and disorders as
			is measured by FMAT using	described in the "Renal
			anti-rat insulin antibodies.	Disorders" section below),
			Insulin secretion from	diabetic neuropathy, nerve
			pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
			disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-

secretion (from pancreatic	hyperosmolar coma.
cells) by polypeptides of the	cardiovascular disease (e.g.,
 invention (including antibodies	
 and agonists or antagonists of	microvascular disease,
 the invention) include assays	hypertension, stroke, and other
 disclosed in: Shimizu, H., et	diseases and disorders as
al., Endocr J, 47(3):261-9	described in the
 (2000); Salapatek, A.M., et al.,	, "Cardiovascular Disorders"
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
17 (1999); Filipsson, K., et al.,	
 Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
 (1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
 Journal of Biomolecular	blindness), ulcers and impaired
Screening, 4:193-204 (1999),	wound healing, and infection
the contents of each of which	(e.g., infectious diseases and
 is herein incorporated by	disorders as described in the
reference in its entirety.	"Infectious Diseases" section
Pancreatic cells that may be	below, especially of the
used according to these assays	urinary tract and skin), carpal
are publicly available (e.g.,	tunnel syndrome and
through the ATCC) and/or	Dupuytren's contracture).
may be routinely generated.	An additional highly preferred
 Exemplary pancreatic cells that	t indication is obesity and/or
may be used according to these	e complications associated with
assays include HITT15 Cells.	obesity. Additional highly
HITT15 are an adherent	preferred indications include
epithelial cell line established	weight loss or alternatively,
from Syrian hamster islet cells	
transformed with SV40. These	preferred indications are

ecils sepress glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981. HSIDJ81 804 Activation of transcription through the transcription through the through NFKB response element are response element in hundry he used or routinely modified as SKNMC cells). Polypeptides of the invention (including antibodies and agonists or antagonists of the invention) modulate expression of neuronal genes. Exemplary assays for transcription throughly Ryr Response heaven and modulate expression of neuronal genes. Exemplary assays for transcription throughly Ryr Ryr Ryr Ryr Ryr Ryr Ryr Ryr Ryr Ry
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routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., Neurobiol Dis, 7(4):448-461 (2000); Tamatani M, et al., J Biol Chem, 274(13):8531- 8538 (1999); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al,	(1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these

				assays include the SKNMC neuronal cell line.	
H	HSKDA27	805	MCP-1 in HUVEC		
H	ISKDA27	805	Production of GM-	GM-CSF FMAT. GM-CSF is	A highly preferred
			CSF	expressed by activated T cells,	embodiment of the invention
				macrophages, endothelial cells,	includes a method for
				and fibroblasts. GM-CSF	stimulating the production of
				regulates differentiation and	GM-CSF. An alternative
				proliferation of granulocytes-	highly preferred embodiment
				macrophage progenitors and	of the invention includes a
				enhances antimicrobial activity	method for inhibiting the
				in neutrophils, monocytes and	production of GM-CSF.
				macrophage. Additionally,	Highly preferred indications
				GM-CSF plays an important	include inflammation and
				role in the differentiation of	inflammatory disorders. An
				dendritic cells and monocytes,	additional highly preferred
				and increases antigen	indication is infection (e.g., as
_				presentation. GM-CSF is	described below under
				considered to be a	"Infectious Disease".
				proinflammatory cytokine.	Highly preferred indications
				Assays for immunomodulatory	include blood disorders (e.g.,
				proteins that promote the	neutropenia (and the
				production of GM-CSF are	prevention of neutropenia
				well known in the art and may	(e.g., in HIV infected patients),
				be used or routinely modified	and/or as described below
				to assess the ability of	under "Immune Activity",
			-	polypeptides of the invention	"Blood-Related Disorders",
				(including antibodies and	and/or "Cardiovascular
				agonists or antagonists of the	Disorders"). Highly preferred
				invention) to mediate	indications also include
				immunomodulation and	autoimmune diseases (e.g.,

		modulate the growth and	rheumatoid arthritis. systemic
		differentiation of leukocytes.	lupus erythematosis, multiple
		Exemplary assays that test for	sclerosis and/or as described
		immunomodulatory proteins	below) and
		evaluate the production of	immunodeficiencies (e.g., as
	-	cytokines, such as GM-CSF,	described below). Additional
		and the activation of T cells.	highly preferred indications
		Such assays that may be used	include asthma. Highly
		or routinely modified to test	preferred indications include
		immunomodulatory activity of	neoplastic diseases (e.g.,
		polypeptides of the invention	leukemia (e.g., acute
		(including antibodies and	lymphoblastic leukemia, and
-		agonists or antagonists of the	acute myelogenous leukemia),
		invention) include the assays	lymphoma (e.g., non-
		disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
-		Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
		204 (1999); Rowland et al.,	described below under
-		"Lymphocytes: a practical	"Hyperproliferative
		approach" Chapter 6:138-160	Disorders"). Highly preferred
		(2000); and Ye et al., J Leukoc	indications include neoplasms
		Biol (58(2):225-233, the	and cancers, such as, leukemia,
		contents of each of which are	lymphoma, melanoma, and
		herein incorporated by	prostate, breast, lung, colon,
		reference in its entirety.	pancreatic, esophageal,
		Natural killer cells that may be	stomach, brain, liver and
		used according to these assays	urinary cancer. Other preferred
	-12	are publicly available (e.g.,	indications include benign
		through the ATCC) or may be	dysproliferative disorders and
		isolated using techniques	pre-neoplastic conditions, such
-		disclosed herein or otherwise	as, for example, hyperplasia,
		known in the art. Natural	metaplasia, and/or dysplasia.

			killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cellmediated cytotoxicity.	Highly preferred indications include: suppression of immune reactions to transplanted organs and tissues (e.g., bone marrow transplant); accelerating myeloid recovery; and mobilizing hematopoietic progenitor cells. Preferred indications include boosting a T cell-mediated immune response. Preferred immune response. Preferred indications include anemia, pancytopenia, leukopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and
HSKDA27	805	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to	allergy. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication

			_											_															
associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment
assess the ability of polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to promote caspase	protease-mediated apoptosis.	Apoptosis in pancreatic beta is	associated with induction and	progression of diabetes.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in: Loweth, AC, et	al., FEBS Lett, 400(3):285-8	(1997); Saini, KS, et al.,	Biochem Mol Biol Int,	39(6):1229-36 (1996);	Krautheim, A., et al., Br J	Pharmacol, 129(4):687-94	(2000); Chandra J, et al.,	Diabetes, 50 Suppl 1:S44-7	(2001); Suk K, et al., J	Immunol, 166(7):4481-9	(2001); Tejedo J, et al., FEBS	Lett, 459(2):238-43 (1999);	Zhang, S., et al., FEBS Lett,
		_											_				-												

(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with inculin associated with	
455(3):315-20 (1999); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include RIN-m. RIN-m is a rat adherent pancreatic beta	derived from a radiation induced transplantable rat islet cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.

HS	HSKDA27	805	Caspase		
			(+paclitaxel) in SW480		
SH	HSKGN81	908	Glucose Production in H4IIE		
HS	HSKGN81	806	SEAP in HIB/CRE		
SH HS	HSKGN81	908	Stimulation of	Assays for measuring secretion	A highly preferred
			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
	_			stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
-				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
	-			Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
-				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
			•	cells) by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,

microvascular disease, hypertension, stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection	(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dunuvtren's contracture).	An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively,	red indic is associa ance.
and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett,	377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein	incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary	pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable inculingman	These cells retain characteristics typical of native pancreatic beta cells including plucose inducible insulin

				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	The state of the s
HSKGN81	3N81	908	IL-8 in SW480		
HSTC	282	807	Activation of	Assays for the activation of	A preferred embodiment of
			transcription	transcription through the	the invention includes a
-			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
			-	antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated

		concentrations of cytosolic	diabetic neuropathy, nerve
		calcium compared to much	disease and nerve damage
		higher extracellular calcium.	(e.g., due to diabetic
		Extracellular factors can cause	neuropathy), blood vessel
_		an influx of calcium, leading to	blockage, heart disease, stroke,
		activation of calcium	impotence (e.g., due to diabetic
		responsive signaling pathways	neuropathy or blood vessel
		and alterations in cell	blockage), seizures, mental
		functions. Exemplary assays	confusion, drowsiness,
		that may be used or routinely	nonketotic hyperglycemic-
		modified to measure calcium	hyperosmolar coma,
_		flux by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Satin LS, et al.,	diseases and disorders as
		Endocrinology, 136(10):4589-	described in the
	-	601 (1995); Mogami H, et al.,	"Cardiovascular Disorders"
		Endocrinology, 136(7):2960-6	section below), dyslipidemia,
		(1995); Richardson SB, et al.,	endocrine disorders (as
		Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
		(1992); and, Meats, JE, et al.,	Disorders" section below),
		Cell Calcium 1989 Nov-	neuropathy, vision impairment
		Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
		contents of each of which is	blindness), ulcers and impaired
		herein incorporated by	wound healing, and infection
		reference in its entirety.	(e.g., infectious diseases and
		Pancreatic cells that may be	disorders as described in the
		used according to these assays	"Infectious Diseases" section
		are publicly available (e.g.,	below, especially of the
-		through the ATCC) and/or	urinary tract and skin), carpal

			may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells correte inculin which is	tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with
			glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981	
НЅQFР66	810	Stimulation of insulin secretion from pancreatic	Assays for measuring secretion of insulin are well-known in the art and may be used or	A highly preferred indication is diabetes mellitus. An additional highly preferred
		beta cells.	routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as

is measured by FMAT using	described in the "Renal
anti-rat insulin antibodies.	Disorders" section below),
Insulin secretion from	diabetic neuropathy, nerve
pancreatic beta cells is	disease and nerve damage
upregulated by glucose and	(e.g., due to diabetic
also by certain	neuropathy), blood vessel
proteins/peptides, and	blockage, heart disease, stroke,
 disregulation is a key	impotence (e.g., due to diabetic
component in diabetes.	neuropathy or blood vessel
Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
 test for stimulation of insulin	nonketotic hyperglycemic-
 secretion (from pancreatic	hyperosmolar coma,
 cells) by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
 and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Ahren, B., et al.,	diseases and disorders as
Am J Physiol, 277(4 Pt	described in the
2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
al., Endocrinology,	section below), dyslipidemia,
138(9):3735-40 (1997); Kim,	endocrine disorders (as
K.H., et al., FEBS Lett,	described in the "Endocrine
377(2):237-9 (1995); and,	Disorders" section below),
Miraglia S et. al., Journal of	neuropathy, vision impairment
Biomolecular Screening,	(e.g., diabetic retinopathy and
4:193-204 (1999), the contents	blindness), ulcers and impaired
of each of which is herein	wound healing, and infection
incorporated by reference in its	(e.g., infectious diseases and
entirety. Pancreatic cells that	disorders as described in the
may be used according to these	"Infectious Diseases" section

				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
-				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
_				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
	-			These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
_				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HSRFZ57	811	Regulation of	Assays for the regulation of	A highly preferred
			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
	-		promoter element	known in the art and may be	indication is a complication
	-		in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the FAS	diseases and disorders as
				promoter element in a reporter	described in the "Renal
				construct and to regulate	Disorders" section below),
				transcription of FAS, a key	diabetic neuropathy, nerve

	enzyme for linogenesis FAS	disease and nerve damage
	nromoter is regulated by many	(e a due to dishetic
	promoter is regulated by many	(c.g., uuc to ataoctic
	transcription factors including	neuropathy), blood vessel
	SREBP. Insulin increases FAS	blockage, heart disease, stroke,
	gene transcription in livers of	impotence (e.g., due to diabetic
	diabetic mice. This	neuropathy or blood vessel
	stimulation of transcription is	blockage), seizures, mental
	also somewhat glucose	confusion, drowsiness,
	dependent. Exemplary assays	nonketotic hyperglycemic-
	that may be used or routinely	hyperosmolar coma,
	modified to test for FAS	cardiovascular disease (e.g.,
	promoter element activity (in	heart disease, atherosclerosis,
	hepatocytes) by polypeptides	microvascular disease,
-	of the invention (including	hypertension, stroke, and other
	antibodies and agonists or	diseases and disorders as
	antagonists of the invention)	described in the
	include assays disclosed in	"Cardiovascular Disorders"
	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	53 (2000); Roder, K., et al.,	described in the "Endocrine
	Eur J Biochem, 260(3):743-51	Disorders" section below),
	(1999); Oskouian B, et al.,	neuropathy, vision impairment
	Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
	(1996); Berger, et al., Gene	blindness), ulcers and impaired
	66:1-10 (1988); and, Cullen,	wound healing, and infection
	B., et al., Methods in Enzymol.	(e.g., infectious diseases and
	216:362–368 (1992), the	disorders as described in the
	contents of each of which is	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety.	urinary tract and skin), carpal
	Hepatocytes that may be used	tunnel syndrome and

			according to these assays, such as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be	Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with
			routinely generated. Exemplary henatocytes that	obesity. Additional highly preferred indications include
			may be used according to these	weight loss or alternatively,
			assays include rat liver hepatoma cell line(s) inducible	weignt gain. Adinonal highly preferred indications are
			with glucocorticoids, insulin,	complications associated with
HSRFZ57	811	Production of	Assays for measuring	Highly preferred indications
		VCAM in	expression of VCAM are well-	include inflammation (acute
		endothelial cells	known in the art and may be	and chronic), restnosis,
		(such as human	used or routinely modified to	atherosclerosis, asthma and
		umbilical vein	assess the ability of	allergy. Highly preferred
		endothelial cells	polypeptides of the invention	indications include
		(HUVEC))	(including antibodies and	inflammation and
			agonists or antagonists of the	inflammatory disorders,
			invention) to regulate VCAM	immunological disorders,
			expression. For example,	neoplastic disorders (e.g.
			FMAT may be used to meaure	cancer/tumorigenesis), and
			the upregulation of cell surface	cardiovascular disorders (such
			VCAM-1 expresssion in	as described below under
			endothelial cells. Endothelial	"Immune Activity", "Blood-
			cells are cells that line blood	Related Disorders",
			vessels, and are involved in	"Hyperproliferative Disorders"
 			functions that include, but are	and/or "Cardiovascular
 			not limited to, angiogenesis,	Disorders"). Highly preferred
			vascular permeability, vascular	indications include neoplasms
			tone, and immune cell	and cancers such as, for

v oq oq					extravasation. Exemplary endothelial cells that may be	example, leukemia, lymphoma, melanoma, renal cell
include human umbilical vein bre endothelial cells (HUVEC), ess which are available from [Iv commercial sources. The pre expression of VCAM be expression of VCAM displayed by cytokines or other factors, and contributes must to the extravasation of hymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoter (antiCD3 expression plays expression plays expression plays expression plays entered or as T-cells).					used according to these assays	carcinoma, and prostate,
which are available from commercial sources. The expression of VCAM be expression of VCAM displayed by cytokines or other factors, and contributes me to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoter (antiCD3 co-stim) 811 SEAP in Jurkat/IL4 promoting immune and inflammatory responses. 812 Activation of transcription through the through serum response element in immune cells (such art and may be used or an immune cells (such art and may be used or in the invention (including in inflamity of polypeptides of in the invention (including in inflamity or in in the invention (including in inflamity or in inflamity or in inflamity or in in the invention (including in inflamity or in in the invention (including in in inthe invention (including in inthe invention (including in inthe intention (including intit))	-				include human umbilical vein	breast, lung, colon, pancreatic,
which are available from commercial sources. The pre expression of VCAM displays a membrane- associated protein, can be copined by cytokines or coupregulated by cytokines or coupregulated by cytokines or coupregulated by cytokines or expected protein, can be commercial sources. However, and contributes mean to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoter (antiCD3 co-stim) 811 SEAP in Jurkat/IL4 promoting immune and inflammatory responses. 812 Activation of transcription through the transcription franscription through serum (SRE) are well-known in the response element in immune cells (such art and may be used or as T-cells). the ability of polypeptides of in the invention (including in					endothelial cells (HUVEC),	esophageal, stomach, brain,
commercial sources. The pre- expression of VCAM (CD106), a membrane- disassociated protein, can be co- upregulated by cytokines or ex- other factors, and contributes may to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoter (antiCD3 co-stim) 811 SEAP in Jurkat/IL4 promoter (antiCD3 co-stim) Activation of Activation of transcription through the thrungh serum response element in (SRE) are well-known in the re- immune cells (such art and may be used or promimum cells (such art and may be used or in the immune cells (such art and may be used or in the ability of polypeptides of in the invention (including fine) antibodies and agonists or in					which are available from	liver and urinary cancer. Other
expression of VCAM displayed (CD106), a membrane-displayed by cytokines or concluded by cytokines or other factors, and contributes me to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoter (antiCD3 co-stim) 812 Activation of Assays for the activation of transcription transcription art and may be used or as T-cells). Rexpression of Assays for the activation of the immune cells (such art and may be used or as T-cells). Rexpression plays a role in promoter (antiCD3 co-stim) Assays for the activation of transcription through the transcription art and may be used or promoter (anticologies and agonists or in in the invention (including for in the invention (including in including including in including including in including i				100	commercial sources. The	preferred indications include
(CD106), a membrane- disassociated protein, can be co upregulated by cytokines or extother factors, and contributes me to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels, thus VCAM expression plays a role in promoting immune and inflammatory responses. 811 SEAP in Jurkat/IL4 promoting immune and inflammatory responses. 812 Activation of Assays for the activation of transcription transcription transcription transcription transcription transcription transcription art and may be used or promume cells (such art and may be used or as as T-cells). The ability of polypeptides of in the invention (including in in the invention (including in in the invention including in in including includi					expression of VCAM	benign dysproliferative
associated protein, can be coupregulated by cytokines or other factors, and contributes me to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses. 811 SEAP in Jurkat/IL4 promoting immune and inflammatory responses. 812 Activation of transcription through the through serum through serum cells (such art and may be used or immune cells (such art and may be used or immune cells (such art and may be used or in the invention (including for antibodies and agonists or in in antibodies and agonists or in in the invention in including in in the invention including in including i					(CD106), a membrane-	disorders and pre-neoplastic
upregulated by cytokines or extother factors, and contributes me to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoter (antiCD3 co-stim) 811 SEAP in Jurkat/IL4 promoting immune and inflammatory responses. 812 Activation of Assays for the activation of transcription transcription through serum (SRE) are well-known in the response element in immune cells (such art and may be used or as T-cells). the ability of polypeptides of in the invention (including for antipodics and agonists or in in antibodics and agonists or in in the invention in the inv					associated protein, can be	conditions, such as, for
other factors, and contributes me to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoter (antiCD3 co-stim) 812 Activation of transcription through the through serum response element in immune cells (such at and may be used or as T-cells). to the extravasation of lymphocytes, leucocytes and expression plays a role in promoter (antiCD3 Acsays for the activation of transcription (SRE) are well-known in the response element in immune cells (such art and may be used or as T-cells). the ability of polypeptides of in the invention (including in					upregulated by cytokines or	example, hyperplasia,
to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses. 811 SEAP in Jurkat/IL4 promoter (antiCD3 co-stim) Activation of transcription through the transcription franscription through the through serum response element in immune cells (such art and may be used or as T-cells). the ability of polypeptides of in the invention (including for antibodies and agonists or in					other factors, and contributes	metaplasia, and/or dysplasia.
lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses. SEAP in Jurkat/IL4 promoting immune and inflammatory responses.					to the extravasation of	
vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses. 811 SEAP in Jurkat/IL4 promoter (antiCD3 co-stim) 812 Activation of transcription through the through serum response element in response element in immune cells (such art and may be used or as T-cells). Response element in the ability of polypeptides of in the invention (including fo					lymphocytes, leucocytes and	
vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses. 811 SEAP in Jurkat/IL4 promoter (antiCD3 co-stim) Activation of Activation of transcription through serum response element in (SRE) are well-known in the immune cells (such art and may be used or as T-cells). the ability of polypeptides of in the invention (including for antibodies and agonists or in					other immune cells from blood	
811 SEAP in Jurkat/IL4 promoting immune and inflammatory responses. 812 Activation of transcription through the through serum response element in immune cells (such as T-cells). 812 Activation of transcription through the through serum serum response element in through serum as T-cells). 813 Activation of transcription through the through serum transcription through the immune cells (such art and may be used or as T-cells). 814 Assays for the activation of the invention (including for in the invention (including in antibodies and agonists or in in the invention (including in intervention (including in in the invention (including in intervention (including intervention (including in int					vessels; thus VCAM	
811 SEAP in Jurkat/IL4 promoter (antiCD3 co-stim) 812 Activation of transcription through the through serum through serum response element in immune cells (such art and may be used or as T-cells). 812 Activation of Assays for the activation of transcription transcription through the through serum serum (SRE) are well-known in the immune cells (such art and may be used or as T-cells). 812 Activation of Assays for the activation of the invention (including for in the invention (including in intervention (including int					expression plays a role in	
811 SEAP in Jurkat/IL4 promoter (antiCD3 co-stim) 812 Activation of transcription through the through serum through serum seponse element in the immune cells (such art and may be used or as T-cells). 814 Assays for the activation of transcription through the through serum through					promoting immune and	
811 SEAP in Jurkat/IL4 promoter (antiCD3 co-stim) 812 Activation of transcription through the through serum response element in (SRE) are well-known in the immune cells (such art and may be used or as T-cells). the invention (including followists or in antibodies and agonists or in incommence or in the invention including in incommence		•			inflammatory responses.	
promoter (antiCD3 co-stim) Activation of transcription through the through serum response element in (SRE) are well-known in the immune cells (such art and may be used or as T-cells). the ability of polypeptides of the invention (including in antibodies and agonists or in		HSRFZ57	811	SEAP in Jurkat/IL4		
transcription through serum response element in immune cells (such as T-cells). Serum Response Element in (SRE) are well-known in the art and may be used or proutinely modified to assess proutinely of polypeptides of in the invention (including for antibodies and agonists or in				promoter (antiCD3 co-stim)		
transcription through serum Serum Response Element response element in (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or		HSSFT08	812	Activation of	Assays for the activation of	A preferred embodiment of
Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or				transcription	transcription through the	the invention includes a
(SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or				through serum	Serum Response Element	method for inhibiting (e.g.,
art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or				response element in	(SRE) are well-known in the	reducing) TNF alpha
routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or		-		immune cells (such	art and may be used or	production. An alternative
<u></u>				as T-cells).	routinely modified to assess	preferred embodiment of the
					the ability of polypeptides of	invention includes a method
					the invention (including	for stimulating (e.g.,
					antibodies and agonists or	increasing) TNF alpha

		antagonists of the invention) to	production. Preferred
_		regulate the serum response	≅
	-	factors and modulate the	disorders (e.g., as described
		expression of genes involved	below under "Immune
		in growth. Exemplary assays	Activity", "Blood-Related
		for transcription through the	Disorders", and/or
	-	SRE that may be used or	"Cardiovascular Disorders"),
		routinely modified to test SRE	Highly preferred indications
		activity of the polypeptides of	include autoimmune diseases
		the invention (including	(e.g., rheumatoid arthritis,
	-	antibodies and agonists or	systemic lupus erythematosis,
		antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
_		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
	_	cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
_		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative

	Iture	s with cytotoxic	. cancers, such as, for example, lenkemia lymphoma	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	
line, whi	depender depender		activity.																										_
										-																			_

				hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HSSGD52	813	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
			development. Exemplary	immunodeficiencies (e.g., as

described below). Preferred indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia		multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,
assays for transcription through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells
						-																							
			_																										

			that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature most cell.	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
HSSGD52	813	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammation and include blood disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
			involved in	immunodeficiencies (e.g., as

<u> </u>	immunomodulatory functions.	described below). Preferred
	Exemplary assays for	indications include neoplastic
 	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
 1	modified to test NFAT-	pancreatic, esophageal,
I	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
9	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); De Boer	Preferred indications include
9	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
9	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
 1	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
 I	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,

through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC- 1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	adipose cells (such increases or decreases) of as 3T3-L1 cells) as 3T3-L1 cells) cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on viable cells in culture based on
	813
	HSSGD52

			off closed of cities to be	
			presence of metabolically	
			active cells. 3T3-L1 is a	
			mouse preadipocyte cell line. It	
			is a continuous substrain of	
			3T3 fibroblast cells developed	
			through clonal isolation. Cells	
			were differentiated to an	
\			adipose-like state before being	
-			used in the screen. See Green	
•			H and Meuth M., Cell 3: 127-	
			133 (1974), which is herein	
			incorporated by reference in its	
			entirety.	
HSSGD52	813	IL-2 in Human T-		
		cell 293T		
 HSSGD52	813	Activation of	Assays for the activation of	A preferred embodiment of
	-	transcription	transcription through the	the invention includes a
		through serum	Serum Response Element	method for inhibiting (e.g.,
		response element in	(SRE) are well-known in the	reducing) TNF alpha
		immune cells (such	art and may be used or	production. An alternative
		as natural killer	routinely modified to assess	highly preferred embodiment
		cells).	the ability of polypeptides of	of the invention includes a
•			the invention (including	method for stimulating (e.g.,
•			antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate serum response	indications include blood
•••			factors and modulate the	disorders (e.g., as described
•		-	expression of genes involved	below under "Immune
		-	in growth and upregulate the	Activity", "Blood-Related
			function of growth-related	Disorders", and/or

				_											-															_
"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma ofioma (e.g.
genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity
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